The Use of High-Resolution Ultrasound and Ultrasound-Guided Needle Core Biopsy in the Diagnosis of Major Salivary Gland Lesions.

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Abstract

Over recent years there have been significant changes in both the diagnosis and management of palpable swellings of the parotid and submandibular major salivary glands. There is a requirement and an expectation from both clinicians and patients that a pre-operative diagnosis is available and that it is accurate and obtained in a manner which is safe and timely, this is of particular importance with the advent of minimally invasive surgical techniques. There is also increasing recognition that the principal current salivary gland biopsy technique, fine needle aspiration cytology (FNAC), is associated with significant drawbacks and is not performing reliably across a network of institutions.

This critical appraisal concentrates on two key areas of my research and utilises eleven published works and numerous selected references to examine and detail the contribution my research has made to changes in modern salivary gland clinical practice. Firstly, the appraisal demonstrates the diagnostic utility of high resolution ultrasound in symptomatic salivary gland evaluation. The included publications and references extend over a twelve year period and when combined with other relevant literature have helped confirm ultrasound as the initial imaging modality of choice in this clinical scenario, with ultrasound now widely used in North America, as well as the United Kingdom and Europe.

The second, and more extensive component of the appraisal, concentrates on the demonstration of the successful implementation of ultrasound guided core biopsy (USCB) as a primary biopsy tool of choice in the salivary glands. Works publications and references are included, spanning the initial and innovative
description of this technique applied to a series of parotid patients in 1999, through to the largest current published series in 2015, where good patient tolerability and high diagnostic accuracy of USCB are confirmed.

This critical appraisal demonstrates the significant and sustained contribution of my research with a clear and defined impact on clinical practice. Changes in salivary gland investigation and diagnosis are confirmed at both national and international level, with evidence of increasing acceptance and utilisation of both diagnostic ultrasound and USCB as the primary investigative tools of choice for salivary gland swellings.
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Declaration

I declare that the research contained in this critical appraisal, unless otherwise formally indicated within the text, is the original work of myself, the author. The appraisal has not been previously submitted to this or any other university for a degree, and does not incorporate any material already submitted for a degree. All included published works for which I am the sole author were entirely my own work: those for which I am the first author or final (senior) author are substantially my own work and solely my own work with reference to material discussed within the critical appraisal document.

Signed:

Dated:
Aims of the Critical Appraisal

The recommended management of major salivary gland lesions has been in a state of flux over the past thirty to forty years with persisting debate as to the optimum management strategy for parotid lesions in particular. Over this time period there have been, however, significant changes and improvements in how salivary gland lesions are managed. This critical appraisal documents the contribution my research has made over a sixteen year period to these alterations in practice and includes a series of eleven supporting published works and also selected references.

The appraisal examines two main areas within pre-operative major salivary gland assessment and diagnosis. The first component documents my research and educational contribution to the published literature covering imaging the salivary glands, with particular reference to the utilisation of high resolution diagnostic ultrasound. Ultrasound is now considered the initial imaging modality of choice in salivary gland assessment in most institutions and the selected works / references in this critical appraisal have been chosen to reflect my on-going and sustained contribution to this change in practice.

The second and more substantial component of the appraisal revolves around the use of ultrasound guided core needle biopsy (USCB) in confirming the histological nature of a salivary gland lesion. Here a more direct link can be made to a practice change, following the publication from 1999 describing the first successful use of this biopsy technique in a series of parotid patients (works publication 4.4) and then a series of papers following an enlarging patient cohort, with now the largest
published series of parotid neoplastic USCB in the world literature (works publication 4.10). USCB does address many of the diagnostic issues that surround FNAC and USCB is now the biopsy technique of choice in many centres.
Background and Overview

1.1 Clinical Presentation

The parotid and submandibular glands comprise the major salivary glands and the investigation and diagnosis of pathology involving these structures is the subject of this critical appraisal. The minor salivary glands, including the sublingual glands, occupy a more diverse range of locations, usually more deeply in the neck and pharyngeal regions and tend to present and to be investigated in a different manner.

Typically a parotid or submandibular tumour presents as a mass, or swelling, in the parotid / pre-auricular or submandibular regions. The majority of parotid tumours are within the superficial lobe and, as with submandibular lesions, they are usually palpable clinically. Parotid deep lobe lesions are generally impalpable and present in a different way, with pain or evidence of local effects such as nerve paresis or dysphagia.

Benign salivary gland tumours tend to be relatively slow growing, painless and non-fixed to adjacent structures. Malignant tumours are more inclined to be hard to palpation, there may be fixity to adjacent structures and skin ulceration, rapid or changing speed of growth, cervical lymphadenopathy and facial nerve paralysis (parotids) are signs all strongly suggestive of malignancy. The malignant grade of the tumour may affect presentation, it is recognised that certain well-differentiated primary parotid malignancies can present in a relatively ‘benign’ manner. Pain is a poor discriminator of benign from malignant disease and overall it is important to recognize that the clinical differentiation of a benign from a malignant tumour and indeed of neoplastic from non-neoplastic disease is unreliable [1].
1.2 Pathology Involving the Major Salivary Glands

The head and neck and the major salivary glands in particular are complex structures histologically, containing not only salivary gland tissue, but also fat, lymph nodes and peripheral nerves, all of which can give rise to benign and malignant tumours. The salivary glands are a potential site for metastatic carcinoma, particularly from primary malignant skin neoplasms. Consequently, a broad range of pathologies are recognised in the salivary glands, inflammatory and benign non-neoplastic lesions are common. Neoplasms are relatively uncommon and the majority of these are benign, although benign:malignant tumour ratios do vary between the different salivary glands.

Primary salivary gland neoplasms have an estimated incidence of 70 – 75 benign and 8 – 14 malignant tumours annually per million population in the United Kingdom [2]. Salivary gland malignancies comprise approximately 5% of cancers of the head and neck, and yet they are the most diverse with at least 24 different types recognised within the 2005 World Health Organisation (WHO) categorisation [3]. Seventy percent of salivary carcinomas arise in the parotid gland [3]. As a rule of thumb 80% of all salivary gland tumours arise in the parotid gland also (the majority are superficial lobe in origin) and of these 80% are benign. The smaller the salivary gland the greater the chance of a tumour being malignant (sublingual > submandibular > parotid). Compared to the parotid the benign to malignant ratio falls in the submandibular glands with a submandibular gland malignancy rate of about 50%.
It is beyond the scope of this critical appraisal to discuss in detail major salivary gland pathology, although some discussion is helpful and relevant as it informs some of the diagnostic difficulties that arise.

Salivary gland tumours can show significant morphological diversity and also cross-over of cytological / histological features between different tumour types and even sometimes within an individual tumour. Hybrid tumours, dedifferentiation and malignant degeneration within a benign tumour all serve to complicate histological analysis and accurate diagnosis [3]. Additionally, as some of the histological tumour subtypes are rare, this can further add to diagnostic difficulty, particularly in smaller pathology departments with less exposure to these tumour types.

Histological grading of malignant salivary gland tumours is important for treatment and prognostication and some (well-differentiated) malignant tumours will require assessment of their capsule and interaction with surrounding glandular parenchyma for accurate diagnosis – these factors become important when considering fine needle biopsy techniques and are discussed later.

Non-neoplastic salivary gland lesions are relatively frequent, they may include acute / chronic sialadenitis, granulomatous disorders (tuberculosis, sarcoidosis) and Sjögren’s syndrome, calculi, benign lymph nodes and benign simple cystic lesions.

A classification of salivary gland neoplasms is included in the 2005 WHO publication [3]. A copy of this summary classification for epithelial tumours is included in the works publication 4.1.
Briefly, salivary gland tumours are divided up into five main categories:

i) **Malignant epithelial tumours**
Including the more common primary malignant tumours: acinic cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma and adenocarcinoma.

ii) **Benign epithelial tumours**
Including the most common benign tumour – pleomorphic adenoma, also Warthin tumour, basal cell adenoma and other less common adenomas.

iii) **Soft tissue tumours**
Including haemangioma, this group would also incorporate other tumour types, such as lipoma and neurofibroma.

iv) **Haematolymphoid tumours**
Including Hodgkin’s lymphoma, diffuse large B-cell lymphoma and the marginal zone B-cell lymphomas (these latter tumours can develop within the salivary gland itself outside of lymph nodes, there is a known association with Sjögren’s syndrome).

v) **Secondary malignancy**
Commonly from head and neck squamous cell carcinoma or malignant skin tumours.

1.3 **The need for change in the management of major salivary gland neoplasms**
The main driver for management change has been the recognition that an accurate and also a pre-operative diagnosis is essential in most patients prior to consideration for major salivary gland surgery. As already described the majority of parotid and submandibular gland lesions present with a clinically palpable mass.
Historically these patients were referred to a surgeon, who might have a head and neck interest, but might equally be a generalist, and following clinical examination lesions were often surgically excised as both a diagnostic and therapeutic manoeuvre. Inevitably this meant that for a significant proportion of patients lesions were either inadequately excised then requiring further surgery, or lesions were excised where surgery would have been better avoided. In recognition of the challenges and complications of surgery in this region there was increasing subspecialisation in head and neck surgery. Many surgeons adopted the practice of initial open biopsy of salivary gland lesions in theatre to decide on further surgery whilst the patient was under general anaesthesia. It became clear, however, that incisional open biopsy, although it could provide a histological diagnosis, had many associated problems – these included the need for general anaesthetic, possible facial nerve damage, bleeding, sialocele and fistula formation and also increased rates of tumour spillage/seeding [5]. In the early 1980s these concerns led to the demise of open biopsy in most centres and about this time there were the first reports of utilisation of fine needle aspiration cytology (FNAC) in obtaining pre-operative head and neck diagnosis. This technique is covered in more detail later, but it is worth noting at this stage the widespread difficulties that have been encountered by FNAC in salivary gland diagnosis, particularly when performed non-guided (“blind”) in the clinic setting as was originally the case in most centres.

During this period of diagnostic surgical excision, open biopsy and “blind” FNAC there was, in addition, a relative under-utilisation of the available imaging techniques (importantly computed tomography (CT), ultrasound and magnetic resonance (MR) imaging) that could assist with lesion characterisation and
demarcation. With the introduction of newer imaging techniques and improvements in existing imaging technology there have also been significant changes in surgical treatment, in particular the relatively recent developments in parotid-sparing surgical techniques such as extracapsular dissection. These are beneficial to patients in that they reduce surgical trauma to the parotid gland in particular and potential complications, they are however dependent on obtaining an accurate pre-operative diagnosis [6,7].

1.4 The importance of pre-operative diagnosis in the management of a major salivary gland lesion

With increasing patient and clinician awareness of the importance of an accurate diagnosis prior to salivary gland surgical intervention, a process of “triple” assessment has developed in many centres, mirroring the system initially developed for breast lesions. This concept involves initial clinical evaluation, imaging and finally cytological/histological diagnosis as needed. It is around the latter two components of the three stage diagnostic process that this critical appraisal revolves – namely the appropriate selection and optimisation of diagnostic imaging modalities and then utilisation of a biopsy technique that is safe, well tolerated, reliable and capable of high levels of diagnostic adequacy and accuracy.

An accurate pre-operative diagnosis is considered essential for several reasons:

- Allows appropriate operative timing and selection.
• Facilitates informed and pre-operative patient consent, particularly important with larger or malignant parotid lesions where facial nerve integrity may be threatened or sacrificed.

• Gives the opportunity for both full tumour staging prior to surgery in malignant lesions and also for the use of adjuvant and neo-adjuvant pre-operative treatments for some malignancies.

• Allows the avoidance of surgery in some tumours (eg. Warthin’s tumour) in the elderly or the unfit.

• Identifies pathology where surgery is best avoided (eg. tuberculosis); demonstrates pseudo-tumourous lesions (ie. a ‘palpable’ lump, but no lesion present on imaging); diagnoses benign and non-neoplastic palpable lesions, eg. Intraparotid retention cyst, calculus, reactive lymph node, where surgery would not usually be indicated.
2. Imaging a Palpable Swelling of the Major Salivary Glands

A variety of imaging modalities have been used for major salivary gland assessment, often in combination and all have relative strengths and weaknesses. A core component of this critical appraisal examines the contribution of selected published works (4.1 – 4.3) and also references [13,14,15,16,22,23,24,25,26] to the acceptance and utilisation of high-resolution ultrasound in major salivary gland assessment and diagnosis.

2.1 High-Resolution Ultrasound

Ultrasound has been historically relatively under-utilised as an imaging modality in the head and neck region, particularly in North America, although this situation has changed over the past 10 - 15 years with increasing appreciation of the advantages of ultrasound [8,9]. The selected works publications and references have played an important role in this change in perception and alteration in clinical practice. The works publications also reflect changes and improvements in ultrasound technology over time and have been supplemented by other author publications [10,11,12]. Ultrasound employs a transducer which generates a sound wave which penetrates soft tissues and is reflected back to the transducer. The type of tissue will dictate whether sound is absorbed, refracted and dispersed or reflected back and the amount of sound reflection/absorption is detected at the transducer and creates an image. There is a pay-off with transducers between penetration and resolution – a lower frequency beam is needed to penetrate soft tissue further, e.g. in the abdomen, which then reduces resolution. As the major salivary glands are superficial the need for depth penetration is reduced allowing higher resolution
images and increased detail appreciation. Ultrasound is safe, non-ionising, portable and relatively inexpensive. High levels of accuracy in lesion characterisation have been demonstrated (works publication 4.2) and ultrasound can also be used to guide needle biopsy. Ultrasound however cannot penetrate bone and is not useful in either the assessment of bone or of structures with bone overlying them. Ultrasound is also highly operator dependent and importantly there is poor visualisation of the parotid deep lobe sonographically due to bony mandibular obscuration. Although capable of a high level of accuracy, ultrasound alone (as with all imaging modalities) cannot predict the nature of all salivary gland pathology. Ultrasound also cannot reliably demonstrate the intra-parotid path of the facial nerve – this again is a problem for all imaging modalities, the nerve is best seen with magnetic resonance imaging, although not routinely. The main intra-parotid vessels are however clearly demonstrated sonographically and the plane of nerve passage inferred passing superficial to the vessels, thereby allowing delineation of superficial from deep parotid lobe and thereby lesion compartmentalisation. Ultrasound as a modality will be discussed in more detail in the first section of works publications.

Ultrasound has several potential roles in salivary gland assessment:

- To ensure that the clinically palpable lesion actually represents an intra-glandular and a real lesion and that this requires biopsy e.g. palpable calculus or reactive intraglandular lymph node can be diagnosed confidently with ultrasound alone and biopsy avoided.
- Ultrasound is used pre-biopsy to both characterise and compartmentalise parotid tumours. If the lesion is confined to the superficial lobe, and the
lesion is confirmed benign on biopsy, then if excision is appropriate parotid sparing surgery/superficial parotidectomy can be performed.

- Diagnostic ultrasound will often demonstrate additional clinically impalpable and significant lesions (works publication 4.2).
- The use of ultrasound allows precise lesion sampling at time of biopsy e.g. if the lesion is complex and solid/cystic then cystic areas can be avoided and diagnostic yield increased with more solid components biopsied.
- Ultrasound will guide the need for further imaging, usually MRI, in large, atypical or probable malignant lesions.

### 2.2 Magnetic Resonance Imaging (MRI)

This technique uses high magnetic field strengths to create an image and has excellent spatial resolution and tissue contrast definition capabilities. MRI is accurate in salivary gland lesion assessment, with similar reported results to ultrasound [1,8] in lesion characterisation and MRI also does not involve ionising radiation. MRI is discussed further within both selected works publications and also references. As a technique MRI is relatively expensive, not always readily available and is associated with significant failure rate due to patient claustrophobia. MRI usually involves the administration of intravenous contrast when utilised in the salivary glands which has the associated risks of nephrotoxicity (in renal impairment) and allergy.

The parotid deep lobe and deeper pharyngeal and parapharyngeal spaces are clearly demonstrated using MRI which is a diagnostic advantage and MRI is the most effective technique at delineating the facial nerve directly and for
demonstrating malignant neural infiltration (adenoid cystic carcinoma) [1,9,13,14].
MR is not useful in assessing calculi or calcifications.

2.3 Computed Tomography (CT)
This has been a historically popular technique for salivary gland imaging particularly in North America and the Far East [15]. Its use has declined however in primary lesion assessment with increasing acceptance of ultrasound and MRI. This critical appraisal demonstrates the important contribution of the selected works publications and references to this change in role for CT. CT has excellent contrast resolution and remains the technique of choice for the detection of calcification and bone erosion, however it is associated with high levels of ionising radiation and usually requires the use of intravenous iodinated contrast for salivary gland imaging with the associated risks of nephrotoxicity and allergy/anaphylaxis. CT remains the technique of choice for lung staging in cases of salivary gland malignancy and is used in acutely ill patients with suspected parotid/submandibular abscess formation as it can acquire a set of data rapidly to include the deep lobe and parapharyngeal spaces.
2.4 Other Imaging Modalities

Plain film and sialography (conventional contrast, CT or MR sialography) have no role in salivary gland tumour assessment, but are still used for the assessment of possible duct stricture or stone (usually after a negative ultrasound study).

PET (positron emission tomography) has a secondary role in salivary gland malignancy and it is increasingly combined with CT as a staging technique. Nuclear medicine studies have a secondary role in evaluating salivary gland function (eg Sjögren’s syndrome).
3. Biopsy Diagnosis of Major Salivary Gland Lesions

As discussed, an accurate diagnosis of a salivary gland swelling is essential to allow appropriate and timely patient management and for neoplasm characterisation lesion cytology/histology is usually necessary. How this biopsy material is best obtained has been, and to some extent remains, controversial. This topic is the focus of the second part of the critical appraisal which describes how selected works publications (4.4 – 4.11) and references [19, 26, 27, 28, 29, 30, 32, 33, 34, 35] have initiated and then contributed to a significant change in biopsy practice, namely, the introduction of ultrasound-guided core biopsy (USCB) and its successful application in the major salivary glands. This section concentrates on FNAC and USCB, but mention will be made of two other less common forms of biopsy. Intra-operative frozen section analysis is a form of open biopsy that has been previously utilised and has recently been re-evaluated [17] and is discussed in more detail in the works publications. It does have potential benefits, it is recognised however that due to the wide variety, complex and often overlapping appearances of salivary gland tumours, that this technique is not generally applicable or appropriate for complex decision making in theatre. It also does not allow informed pre-operative patient consent and may put unacceptable strains on histopathology departments. Punch biopsy is a further biopsy technique that is sometimes used for submandibular space lesions and is discussed in paper 4.9 in the works publications. This leaves the two principal pre-operative biopsy techniques currently being utilised, both using a small bore needle – namely fine needle aspiration cytology (FNAC) and core biopsy, this usually performed with ultrasound guidance – ultrasound guided core biopsy (USCB).
3.1 Fine Needle Aspiration Cytology (FNAC)

This technique developed following the demise of open biopsy in the 1980s. It involves the use of a small bore needle without local anaesthesia, usually 20G or smaller, with sampling of the lesion in question and the sample smeared on slides and sent to for cytological analysis. Traditionally FNAC was undertaken by clinicians, usually in clinic and performed “blind” i.e. non-guided. FNAC as a technique is fast, cheap and safe. There have been numerous studies looking at the diagnostic performance of FNAC, many reporting high sensitivity and specificity. However, it has become increasingly clear (and the subject of a recent large meta-analysis [18]) that there is a wide variety in the diagnostic performance of FNAC across centres, with high reported non-diagnostic, false negative and false positive rates [19] and also low diagnostic accuracy in FNAC cases reported as non-neoplastic and benign [18].

The performance of FNAC is affected and can be improved by a number of factors [18]: -

- Reduced number of trained operators undertaking the procedure, rather than a wide spectrum of operators of variable experience.
- Cytologist/cytology technician either performing FNAC with the option of repeat sampling or available at the time of FNAC to ensure an adequate sample has been obtained.
- The provision of ancillary cytology facilities, such as flow cytometry or in-situ hybridisation techniques, to improve diagnostic performance.
- The use of ultrasound-guidance to improve sampling accuracy.
However, not all these options are generally available, in particular, in the UK, there are shortages of trained cytologists and cytology technicians and ancillary equipment is expensive and access is restricted. Even where optimised circumstances do exist to improve the sampling performance of FNAC, there are inherent problems for a technique which provides a cellular aspirate in the salivary glands, as already alluded to. Salivary gland tumours have a wide variation in architectural and cytomorphonuclear features and many of these features overlap making cytological analysis difficult. Squamous or mucinous metaplasia, for example, is common in a range of both benign and malignant tumours, and lymphoid hyperplasia is also not reliably diagnosed on FNAC. FNAC cannot provide information on tumour grade, tumour margins or interaction of tumour with adjacent tissue. The diagnostic limitations of FNAC are discussed in more detail later in the critical appraisal, in particular works paper 4.11. Heterogeneity in provision of optimisation resources in part explains the reported variability of performance of FNAC, however, the limitations imposed by a cellular aspirate are more fundamental. The perceived and reported limitations of FNAC have lead interested clinicians to explore other biopsy techniques to improve diagnostic yield.

3.2 Ultrasound Guided Core Biopsy (USCB)

USCB involves the use of a spring-loaded biopsy device that discharges a small bore needle and obtains a core of tissue contained in a central biopsy tray in a single automated movement. Ultrasound is a “real-time” modality and when performing biopsy the probe, needle and patient can all be actively positioned to facilitate safe needle access. Originally USCB was described in the abdomen/liver and breast and demonstrated superior performance over FNAC in these areas.
where USCB is now the technique of choice. Core biopsy uses a larger needle than FNAC, usually 18G in salivary gland work – an 18G needle is 1.2 mm thick and crucially USCB obtains a core of tissue that can be sent for immunohistochemical analysis, rather than relying on a needle aspirate of cells. This additional histopathological facility allows both typing and grading of tumours and also improved characterisation of lymphoid proliferation, namely the differentiation of reactive nodal hyperplasia from low-grade lymphoma [20, 21]. A core of tissue allows assessment of tissue architecture, avoiding the broad category diagnoses associated with FNAC such as “malignant” or “favour neoplasm” and giving a precise and definitive diagnosis. An intact core of tissue will also allow diagnosis of salivary involvement by systemic disease processes. Core biopsy offers increased potential to assess lesion capsular integrity and infiltration of surrounding tissues, although this is an area that remains difficult to evaluate in some cases (discussed in works publications).

Core biopsy does have potential weaknesses when compared to FNAC which are mentioned here and discussed in more detail later in the works publications.

- Minimally more invasive than FNAC with a larger bore needle and requiring local anaesthesia and a small skin incision.
- There is a potentially increased risk of tumour seeding with the larger bore needles used in USCB when compared to FNAC [20,21].
- Not as widely available as FNAC, currently fewer trained operators
- Theoretical increased risk of vascular/nerve injury and bleeding using a larger needle than FNAC – this is more of an issue in the parotids.
• As there is a built-in delay around histological reporting of USCB specimens, USCB does not lend itself to proposed “one-stop” clinic scenarios which revolve around FNAC as a diagnostic tool.

• Potentially more expensive than FNAC as the procedure is a little more complex and time consuming.
3.3 The technique of Ultrasound-Guided Core Biopsy (USCB)

Figure 1 – An image demonstrating a biopsy gun currently used for USCB and an 18 gauge needle alongside. This biopsy device has a variable throw facility of either 15mm or 22mm.

Figure 2
Figures 2 and 3 – These 2 images demonstrate USCB of the left parotid gland in progress. The angle of approach to the parotid can be clearly seen with the transducer in this case aligned longitudinally and parallel to the ear.

(This patient gave written consent for these images to be used for educational and publication purposes).
Figures 4 and 5 - These images are longitudinal sonograms of the left parotid gland (same patient as figure 2) – they demonstrate an atypical intra-parotid lymph node (node outlined by callipers, normal parotid gland – P). Note the line of the mandibular ramus deep to the parotid (M) – there is no sound penetration of the bony mandible, hence lack of any deeper tissue characterization and acoustic shadowing only. In the second image the USCB needle has been deployed and can be seen traversing, but not exiting, the node (arrows N – Needle).

The depth of biopsy device needle throw selected in this case was 22mm – the needle tip is carefully positioned prior to discharge such that once the needle is deployed (22mm throw) it traverses, but does not exit, the lesion. This reduces the potential for damage to deeper structures. The smaller needle throw (15mm) is useful where space is confined, although core samples are often less satisfactory.

Biopsy needles do exist which allow manual extension of the needle biopsy tray with control for depth of penetration, with the outer needle sheath deployed when the operator is satisfied with biopsy tray positioning.
Figure 6 – A close up image of the core sample obtained in the previous case (figures 2 - 5). The sample can be seen within the biopsy tray which has been revealed by retracting the overlying needle sheath after the procedure.
Figure 7 – This figure shows macro histological images of the cores obtained from the previous case to give an idea of what a core sample looks like at low magnification under the microscope and the amount of tissue a core sample can obtain for diagnosis. The final diagnosis in this case was parotid non-Hodgkin’s lymphoma.
Figure 8, 9 – These are two histological images from USCB cases at a higher magnification to demonstrate what USCB samples look like to the pathologist – note the preservation of architecture in the biopsy, improving typing and grading of tumours, this material can also be sent for immunohistochemical analysis.

Figure 8 - H and E stain x200 magnification, is a Warthin’s tumour with central lymphoid cells and bi-layered pink oxyphilic epithelium on the right and left.
Figure 9 - a well differentiated mucoepidermoid carcinoma – H and E stain, x200 magnification – note mucinous cells (on the left) and squamoid epithelium (on the right).
Newer biopsy needles are becoming available which offer several advantages over the current available biopsy devices. Newer generation needles:-

- Employ a side cutting, not end cutting, mechanism which reduces potential distal structure needle trauma.
- Increased throw variations are available – eg. 13, 23, 33mm
- Due to changes in internal needle design a needle of a certain gauge can deliver a larger needle sample – eg. a 18G size needle can deliver an equivalent 16G core, which is helpful for histology and delivers more tissue for diagnosis, with a smaller biopsy hole and reduced trauma.
- Newer needles are disposable after a single use, improving infection control aspects (current needles are likewise single use, but the gun is used repeatedly, ideally requiring cleaning between patients).
- The main downside of the newer needles types is that of cost – typically about £120 per needle compared to approximately £15 for a current needle for example (current biopsy device about £800 as a single purchase), and this is a rate-limiting step for their more widespread introduction.
4. Discussion of Selected Published Works Included in this Critical Appraisal

The selected works publications, eleven in total, are divided into two sections where the salient findings are discussed, together with an analysis of their contribution to the published literature and current clinical practice –

a) The initial three publications (4.1 - 4.3) examine the use of ultrasound in salivary gland assessment and diagnosis.

b) The remaining eight papers (4.4 - 4.11) study the performance, current and future potential roles of USCB in major salivary gland diagnosis.
a) Diagnostic Ultrasound in Major Salivary Gland Assessment

4.1 Mandalia U Y, Porte F N, Howlett D C
Salivary Gland: Oncologic Imaging.
Ultrasound Clinics of North America 2014; 9; 99-113

4.2 Sriskandan N, Hannah A, Howlett D C
A Study to Evaluate the Accuracy of Ultrasound in the Diagnosis of Parotid Lumps and to Review the Sonographic Features of Parotid Lesions – Results in 220 Patients.
Clinical Radiology 2010; 65:366-372

4.3 Westerland O, Howlett D C
Sonoelastography Techniques in the Evaluation and Diagnosis of Parotid Neoplasms
European Radiology 2012; 22 (9) 66-969
b) The Use of Ultrasound Guided Core Biopsy (USCB) in the Histological Diagnosis of a Major Salivary Gland Lesion

4.4 Buckland J R, Manjaly G, Violaris N, Howlett D C
Ultrasound Guided Cutting Needle Biopsy of the Parotid Gland
Journal of Laryngology and Otology 1999; 113; 988-992

4.5 Keese KW, Manjaly G, Violaris N, Howlett D C
Ultrasound Guided Biopsy in the Evaluation of Focal Lesions and Diffuse Swelling of the Parotid Gland.
British Journal of Oral and Maxillofacial Surgery 2002; 40; 364-368

4.6 Howlett D C
Diagnosing a Parotid Lump: Fine Needle Aspiration Cytology or Core Biopsy?

4.7 Howlett D C, Menezes LJ, Lewis K, Moody AB, Violaris N, Williams M D
Sonographically Guided Core Biopsy of a Parotid Mass
American Journal of Roentgenology 2007; 188-223-227

4.8 Breeze J, Andi A, Williams M D, Howlett D C
The Use of Fine Needle Core Biopsy Under Ultrasound Guidance in the Diagnosis of a Parotid Mass

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Evaluation of Biopsy Methods in the Diagnosis of Submandibular Space Pathology.

Diagnostic Investigation of Parotid Neoplasms – a 16 Year Experience of Freehand Fine Needle Aspiration Cytology and Ultrasound Guided Core Biopsy.

4.11 Howlett D C, Skelton E, Moody AB
Establishing an Accurate Diagnosis of a Parotid Lump: An Evaluation of Current Biopsy Methods – Fine Needle Aspiration Cytology, Ultrasound Guided Core Biopsy and Intra-operative Frozen Section.
British Journal of Oral and Maxillofacial Surgery – accepted for publication August 2014
a) Diagnostic Ultrasound in Major Salivary Gland Assessment

4.1. Salivary Gland: Oncologic Imaging

This paper was published in 2014 in the North American journal, Ultrasound Clinics of North America, a journal dedicated to updates and reviews of current ultrasound best practice. This review article contains a detailed and comprehensive examination of the ultrasound features of salivary gland neoplastic disease utilising the most up-to-date sonographic technology. This selected works publication is supplemented by a series of published ultrasound opinion papers and pictorial imaging reviews from over a twelve year period as detailed in the References section [22,23,24,25]. These articles have informed radiological practice supplementing articles from other authors and have encouraged the wider use and acceptance of ultrasound, which now represents the imaging modality of choice in the initial assessment and diagnosis of major salivary gland lesions in most institutions.

The publication of this 2014 paper (4.1) in a North American journal was important – traditionally ultrasound has been relatively under-utilised in North America, where there has been a tendency to rely upon MRI / CT. This publication was extremely encouraging, suggesting an increased understanding and uptake of ultrasound by the North American audience.

Paper 4.1 and also the selected references provide an overview and illustration of the ultrasound findings in salivary gland disease over a prolonged period, incorporating improvements in ultrasound technology and they give a clear demonstration of the importance of ultrasound in the diagnostic pathway.
4.2 A Study to Evaluate the Accuracy of Ultrasound in the Diagnosis of Parotid Lumps and to Review the Sonographic Features of Parotid Lesions – Results in 220 Patients.

This was another important paper published in 2010 in the leading UK based radiology journal, Clinical Radiology, which aimed to assess the accuracy of initial sonographic diagnosis and also to review the sonographic features of parotid lesions when compared to final histology. The paper included 220 patients with data collected over an 11 year period. This published series remains the largest of its kind in the World literature.

A variety of ultrasound machines were employed over the 11 year study period, which affected, at least in part, the diagnostic capabilities of ultrasound as the technology improved. This paper established a diagnostic accuracy of ultrasound in the determination of malignancy of 93%, results not dissimilar to previous smaller published series and comparable to MRI. The paper also highlighted the ability of ultrasound to differentiate benign from malignant disease in most patients and to detect additional lesions impalpable clinically. However, false negative and false positive findings of ultrasound were described and a cross-over of sonographic findings was demonstrated between some benign neoplasms and also between certain benign and malignant neoplasms. The article confirmed ultrasound as a valuable adjunct to clinical examination within the triple assessment pathway, able to characterise and compartmentalise lesions accurately in most patients. However to maximise diagnostic yield it was recommended that ultrasound should be combined with needle biopsy as appropriate.
The paper won the Clinical Radiology Ellis-Barnett prize in 2010 for “best paper published on Ultrasound” that year in the journal.

4.3 Sonoelastography Techniques in the Evaluation and Diagnosis of Parotid Neoplasms.

This was an invited expert review and opinion article, the invitation from the Editor in Chief of European Radiology, the leading European radiology journal publication. This paper provides a critique of two proffered publications to be published in the journal, investigating two novel ultrasound applications in parotid neoplasm assessment. The two papers looked at variations of the technique of sonoelastography: essentially this involves manual compression of tissue applied by an ultrasound probe and the degree of tissue deformation/stiffness is detected and characterised. It was hoped that the technique measuring tissue compliance or stiffness would improve the diagnosis of parotid neoplasia, namely malignant lesions are “stiffer”. Neither technique however was found to offer significant new diagnostic information to existing ultrasound techniques, although a potential advantage over conventional ultrasound was postulated, with a recommendation to undertake larger follow up prospective studies.

This paper is included within the thesis as it demonstrates a published contribution not only to current ultrasound best practice, but also to potential future developments in the technique.
**b) The Use of Ultrasound Guided Core Biopsy (USCB) in the Histological Diagnosis of a Major Salivary Gland Lesion**

### 4.4 Ultrasound-Guided Cutting – Needle Biopsy of the Parotid Gland

This publication is likely to represent the single most important and potentially influential paper contained within this critical appraisal. This article was published in the leading UK clinical ear, nose and throat journal – The Journal of Laryngology and Otology and describes the novel and successful application of USCB to a series of patients with parotid lesions.

In clinical practice most referrals for salivary lump investigation originate from either Ear, Nose or Throat or Oral/Maxillofacial surgeons. At the time of the paper clinician “blind” FNAC was the norm in my institution, with high non-diagnostic rates and a high number of patients undergoing surgical excision for diagnosis. It was clear that changes were necessary to provide an accurate pre-operative diagnosis for patients thereby facilitating appropriate operative management. On review of the existing literature on core biopsy in the abdomen and breast it seemed rational and reasonable that this technique could potentially translate itself safely and effectively to the major salivary glands.

In paper 4.4, 16 patients were included, all had parotid lesions and 13/16 had a previous non-diagnostic blind FNAC. USCB was undertaken with an older type of spring-loaded biopsy gun with a fixed 20mm throw, 18G needles were used in all cases. The range of pathologies encountered is included in the paper.

Key findings from this study:
4. USCB using local anaesthesia was well tolerated by all patients, with no significant complications.

4. There was high diagnostic yield with all samples adequate for histological analysis and with 100% diagnostic accuracy in the seven patients who had subsequent surgery, nine patients therefore avoided surgical excision biopsy on the basis of their USCB biopsy result.

4. Ultrasound detected additional significant clinically occult disease in 31% of cases.

This paper was important – it was the first publication in the world literature describing the use of USCB applied to the parotid glands in a series of patients, previous reports were sporadic, isolated cases. The paper confirmed USCB could be performed safely in the parotid glands and that it offered potential significant diagnostic benefits when compared to FNAC and this work was presented at national surgical and radiological meetings. Over the next few years a series of correspondence type articles discussing and highlighting the potential benefits of USCB were also published and these are included in the References section [26 - 30]. A further paper confirmed that ultrasound alone was sufficient as a pre-operative imaging modality for superficial lobe benign parotid tumours [31].

4.5 Ultrasound Guided Biopsy in the Evaluation of Focal Lesions and Diffuse Swelling of the Parotid Gland

This paper was published in 2002 in the UK based British Journal of Oral and Maxillofacial Surgeons. The paper looked at core biopsy performance and
accuracy in a cohort of 54 patients with parotid swelling (including the original group of 16 patients). USCB was 100% accurate in the differentiation of benign from malignant disease in the 28 patients who had subsequent surgery and histological correlation. These findings were extremely encouraging, there were also no significant biopsy related complications and there was no evidence of tumour seeding at biopsy sites in the clinical follow up period. The paper acknowledged that tumour seeding can occur up to 20 years following parotid instrumentation and the follow-up period for these patients was short. Interestingly clinician performed blind FNAC had effectively ceased in the institution at this stage after the initial publication (4.4) had confirmed the safety and efficacy of USCB.

4.6 Diagnosing a Parotid Lump: Fine Needle Aspiration Cytology or Core Biopsy.

This paper was a review/opinion article published in the British Journal of Radiology. From a literature review and personal experience of both USCB and FNAC it was becoming clear that USCB did potentially offer significant advantages over FNAC in salivary gland diagnosis, advantages that were also becoming apparent in biopsy series of cervical lymphadenopathy [32,33,34]. This British Journal of Radiology paper was the first publication in the peer-reviewed literature where the argument for potential use and selection of USCB over FNAC was made. The paper also effectively argued against NICE (National Institute of Clinical Excellence) guidance published at the time which advocated a “one stop” neck lump service based on the use of FNAC, proposing patients to be
seen, examined, imaged, biopsied and diagnosed in one prolonged clinic attendance. A further related publication at this time commented on the potential disadvantages of the “one stop” model, advocating instead increased utilisation of diagnostic ultrasound and USCB in neck lump assessment, especially in units with poor results from FNAC [35].

4.7 Sonographically Guided Core Biopsy of a Parotid Mass

For USCB as a technique this was another important and landmark publication, published in the North American radiology journal, the American Journal of Roentgenology. The paper contained continuation and new patient data from the original parotid USCB series, with a total of 135 patients included (data from 1998-2004). This was not only the first publication of dedicated USCB parotid data in a radiology journal, but first also in the North American literature and this was the largest published series of parotid USCB patients in the literature at that time. In this paper USCB showed itself to be highly accurate in the diagnosis of a range of both neoplastic and non-neoplastic parotid gland pathology. All biopsies were considered satisfactory for histological analysis. In 74 of the 76 patients who underwent surgery there was biopsy correlation with final surgical histological findings. In the 2 discrepant patients there was malignancy diagnosed in each case at USCB, only the sub-type of malignancy differed between USCB and surgical histology, patient management was unaffected. Fifty-nine patients were diagnosed and managed on USCB results alone, thereby avoiding surgery. Interestingly in this paper there were 17 cases with a USCB diagnosis of Hodgkin’s disease or non-Hodgkin’s lymphoma. Lymphoma, as previously
discussed, is not usually possible to diagnose/characterise on FNAC results and such cases would normally have needed to progress to surgical excision for definitive diagnosis and instigation of treatment. In this paper it was shown that 11/17 cases were diagnosed and treated on the bases of USCB results alone, only 6 cases requiring surgical excision. These findings in lymphoma patients demonstrate not only the good sample yield obtained at USCB, but importantly also increased understanding, familiarity and acceptance of USCB samples and results by histopathologists and treating clinicians. USCB was also well tolerated by patients in the series, it was performed quickly as an out-patient procedure, with no significant complications and with no reported tumour seeding in the biopsy series to date.

4.8 The Use of Fine Needle Core Biopsy Under Ultrasound Guidance in the Diagnosis of a Parotid Mass

This was a follow-up study published in the British Journal of Oral and Maxillofacial Surgeons as a technical procedural note. This was a valuable paper as it confirmed the optimised procedural and technical aspects of biopsy – a modified and upgraded automated biopsy device was now available which was capable of varying the throw of the biopsy needle – a 15 or 22mm throw could be selected, (see earlier). This paper included updated biopsy data in 200 patients, an additional 65 patients to the previous North American journal publication (4.7). In most cases an 18G needle was utilised with an average of two needle passes per patient. USCB again performed extremely well – in 198/200 patients samples were considered suitable for histological analysis, with a diagnostic accuracy of
99.1% and 1 non-correlation – (a false negative) between USCB and final surgical histology.

These results are of interest as they were the first inadequate and also false negative samples in the case series.

The two non-diagnostic cases both had subsequent surgery and were parotid tumours, one a Warthin’s tumour and one an adenocarcinoma – these lesions had been largely cystic on ultrasound explaining the difficulty in obtaining a diagnostic solid sample. The false negative case was in a 28 year old male with a 4 month history of a slowly enlarging, although hard, right parotid mass – ultrasound suggested likely malignancy and USCB had been undertaken and histology suggested likely benign basal cell adenoma. This patient had also had a blind FNAC in clinic pre-USCB – this had reported a pleomorphic adenoma. It is interesting that the clinician still sent the patient for USCB despite having performed FNAC and without knowledge of the FNAC results suggesting a lack of trust in FNAC. Final surgical histology from superficial parotidectomy confirmed a well differentiated basal cell adenocarcinoma, this was only diagnosable once the pathologist could observe the entire resected specimen and could visualise focal capsular infiltration consistent with malignancy. The lesion was completely excised but the patient did proceed to completion parotidectomy with post-operative radiotherapy. This false negative case was educational and highlighted a potential pitfall for USCB – already well recognised with FNAC in the literature – a well differentiated salivary gland malignancy can be difficult to diagnose on needle sampling alone as capsular loss of integrity can be important for diagnosis and may not be apparent on a needle biopsy. In this case there was already a high
clinical/sonographic index of suspicion in the other two limbs of triple assessment. No significant complications had been observed in the series to date – one patient had experienced a small haematoma post-biopsy, no patients had demonstrated tumour seeding (tumour seeding is discussed in more detail in works publication 4.11). The option for surgeons to excise the needle biopsy tract at the time of surgery is available to reduce the potential for tumour seeding and occurs in some centres, although this has not been considered necessary in our institution and there is no evidence to suggest this approach is routinely required.

4.9 Evaluation of Biopsy Methods in the Diagnosis of Submandibular Space Pathology

This paper was published in 2014 in the International Journal of Oral and Maxillofacial Surgery and records the performance of three biopsy techniques in diagnosing pathology of the submandibular space/gland from 1999-2011. Submandibular gland tumours are far less common than parotid tumours, comprising 10-15% of all salivary gland tumours. This study included biopsy data in 44 patients, the relatively small number of patients reflecting the rarity of tumours in this region. Biopsy techniques included clinician performed blind FNAC, USCB and also punch biopsy, a technique that is sometimes used in the submandibular region and is performed in theatre by the surgeon under local anaesthesia. The total of 81 biopsy specimens in the study represents the largest such series in the published literature, with a paucity of previously published work on this subject. FNAC in this series was diagnostic in only 2/15 cases, USCB in 20/24 and punch biopsy in 5/7. USCB was accurate in diagnosing submandibular
space pathology, although a higher proportion of non-diagnostic (2/24) or equivocal (2/24) cases was observed then in the parotids, the reasons for this are unclear. An accurate pre-operative diagnosis is important in the submandibular glands also, this allows informed patient consent and appropriate operative intervention in malignancy. However the submandibular gland is relatively straightforward to excise with no major intraglandular vessels or nerves and if a lesion is present in the gland operative excision can be undertaken as a diagnostic procedure if other biopsy techniques have failed.

4.10 Diagnostic Investigation of Parotid Neoplasms – a 16 Year Experience of Freehand Fine Needle Aspiration Cytology and Ultrasound Guided Core Needle Biopsy.

This publication is the tenth works publication, it was published in the International Journal of Oral and Maxillofacial Surgery in early 2015. This paper reviews all parotid neoplasm biopsy data on the updated cohort of patients in Eastbourne performed over a 16 year period. Three hundred and ninety-eight patients are included, all with parotid tumours and including 313 USCB specimens, the largest parotid USCB series in the current world literature. This paper does differ in two aspects from previous publications in the thesis – only parotid neoplasms are included, non-neoplastic biopsies are excluded and FNAC data and primary diagnostic surgical excision (direct surgical removal with no pre-operative biopsy diagnosis) data is included along with data from USCB. This paper does not attempt to make a direct comparison between USCB and FNAC.
FNAC in all cases had been performed blind by clinicians and was not being undertaken under the optimised circumstances already alluded to that can increase the diagnostic yield. However, this situation probably does reflect actual clinical practice in many institutions and the performance of blind FNAC did merit recording and comment. USCB recorded a 4.2% non-diagnostic rate, sensitivity of 93% and specificity of 100% in the surgical group. There was a further false negative USCB result – a different pathology to the previous case (paper 4.8) but a not dissimilar explanation. This case was rare, a well-differentiated parotid malignancy (myoepithelial carcinoma) and USCB reported a likely basal cell adenoma or benign myoepithelioma. Histological examination of the integrity of the capsule of the entire resected specimen was necessary for a final malignant diagnosis.

One hundred and thirty two patients with a parotid neoplasm had their final diagnosis confirmed with USCB and avoided surgery – the majority of these patients had Warthin’s tumours, the remainder were elderly, unfit, had metastatic disease or simply declined resection. It can be seen within the paper that the use of surgical excision biopsy (and FNAC) as the primary diagnostic tool had reduced significantly over time, reflecting increased acceptance and utilisation of USCB. The results of FNAC are recorded in the paper, the most striking figure is that of a 56% non-diagnostic rate. Several meta-analyses have been recently published, already alluded to in this thesis, looking at the published performance of FNAC [18] but also of USCB [20] with a supplementary paper updating USCB data published in 2014 [21] in addition to the initial 2011 publication [20]. The 2014 [21] paper includes information from 12 published series (paper 4.10 is not included), a smaller number than available FNAC publications, but still considered by the
authors to be representative and applicable to USCB across a wider network of institutions. USCB was shown to have no significant heterogeneity in performance across centres when compared to FNAC, also a reduced non-diagnostic and false negative rate and improved diagnostic accuracy. The paper suggested that USCB should be considered as the diagnostic alternative to FNAC particularly in institutions where FNAC performed poorly on audited results.

4.11 Establishing an Accurate Diagnosis of a Parotid Lump: An Evaluation of the Current Biopsy Methods – Fine Needle Aspiration Cytology, Ultrasound – Guided Core Biopsy and Intra-Operative Frozen Section.

This is the eleventh and final selected works publication within the critical appraisal, accepted for publication in August 2014 in the British Journal of Oral and Maxillofacial Surgery. This is a review/opinion article which examines the current literature surrounding the performance of the currently described parotid biopsy techniques. FNAC and USCB, but also includes discussion around intra-operative frozen section following several recent publications supporting this technique. The paper refers in detail to the content of recent published meta-analyses looking at performance of FNAC, USCB and frozen section [17,18,21]. As already discussed FNAC may perform poorly even when a cellular aspirate is obtained and underperformance can also occur even when a cytologist can offer repeat sampling [36]. A large series of parotid frozen section cases was published in 2013 [37] with 1339 cases and describing sensitivity of 98.5% and specificity of 99% and the authors proposed this technique as an intra-operative decision making tool. Fakhry et al [36] likewise suggested frozen section as a confirmatory
tool in cases of equivocal or non-diagnostic FNAC. Interestingly in the 2013 publication [37] the authors mention that FNAC is rarely performed in their institution (presumably due to problems with the technique) and neither publication makes any mention of USCB – which is surprising.

In reality, it is hard to recommend the use of intra-operative frozen section as a primary diagnostic tool for most patients. An accurate and pre-operative diagnosis represents the ideal for most clinicians and their patients for reasons already discussed. Intra-operative frozen section shares the concerns associated with traditional open biopsy and is also not a procedure most pathologists find acceptable due to the pressures of reaching a potentially difficult diagnosis whilst the patient is anaesthetised. Frozen section does have definite advantages for a minority of patients as it does allow more accurate diagnosis of capsular or local invasion. A role can certainly be postulated for frozen section / excision of parotid deep lobe lesions not amenable to percutaneous biopsy, or where FNAC/USCB are felt to be non-representative for a superficial parotid lesion. Frozen section is not the answer to underperforming FNAC, the solution to this, in most cases, should be USCB (if available). Paper 4.11 concludes by suggesting the USCB is likely to supplant FNAC as the primary diagnostic tool of choice in the major salivary glands, however, an increase of USCB trained operators is likely to be necessary to enable this.
5. Conclusion

This critical appraisal demonstrates how a selection of my published works over 16 years, from 1998-2014, have helped inform and improve the diagnosis of major salivary gland swellings. The works publications and selected references pertaining to ultrasound as a diagnostic technique have contributed significantly to the published literature, supporting ultrasound as the initial imaging modality of choice in the evaluation of symptomatic parotid and submandibular glands. The second and larger component of the critical appraisal concentrates on the use of USCB in making both an accurate and pre-operative histological diagnosis of major salivary gland lesions, including the first description of the technique successfully applied to a series of parotid patients, through to safe and accurate results in the largest current published cohort of parotid neoplasia. Recent published meta-analyses have confirmed the limitations of FNAC even under optimised circumstances and have supported the use of USCB as a biopsy technique of choice. There is evidence of increasing utilisation of USCB worldwide with published data supporting high levels of diagnostic accuracy and patient tolerability of this technique. The improvements in accuracy of USCB when compared to FNAC will result in accelerated diagnosis and facilitate appropriate and timely patient treatment – these benefits are likely to outweigh any additional financial costs of USCB when compared to FNAC. It is likely, from personal experience and informed by the published literature, that over time USCB will largely replace FNAC as the diagnostic biopsy technique of choice for major salivary gland lesions in many institutions, replicating what has already occurred in breast practice. For this to occur there will be resource issues
with appropriate staffing and training needed to provide more widespread USCB facilities, it is entirely possible in the future that ultrasound and USCB may be provided by suitably qualified clinicians, other than radiologists, in appropriate circumstances.
6. References

[1] Silvers AR, Som PM
Salivary Glands
Radiologic Clinics of North America 1998; 36 (5); 941-966

British Journal of Oral and Maxillofacial Surgery 2013; 51: 399-403

[3] Eveson JW, Auclair PL, Gnepp DR et al
Tumours of the Salivary Glands: Introduction.

Salivary Neoplasms: Overview of a 35 year Experience with 2807 Patients.
Head and Neck Surgery 1986; 8: 177-184

Incisional or Core Biopsy of Salivary Gland Tumours: How Far Should We Go?
Diagnostic Histopathology 2012; 18(9): 358-365

Pleomorphic Adenoma of the Parotid Gland; Formal Parotidectomy or Limited Surgery?

[8] Orioff LA, Hwang HS, Jecker P
The Role of Ultrasound in the Diagnosis and Management of Salivary Gland Disease.
Operative Technology Otolaryngology and Head and Neck Surgery 2009; 20 (2): 136-144

[9] Lee YY, Wong KT, King AD
Imaging of Salivary Gland Tumours.
Characteristic Sonographic Findings of Warthin’s Tumour of the Parotid Gland.
Journal of Clinical Ultrasound 2004; 32; 78-81

Role of Ultrasonography in Diagnosis and Differentiation of Pleomorphic Adenomas: Work in Progress
Archives of Otolaryngology and Head and Neck Surgery 2003; 129: 929-933

[12] Bialek EJ, Jakubowski W, Zajkowski P
Radiographics 2006; 26: 745-763

An Unusual Cause of Facial Pain: Malignant Change in Calcified Pleomorphic Adenoma in the Deep Lobe of the Parotid Gland
Ear, Nose and Throat Journal 2003; 82; 623-625

[14] Breeze J, Ramesar K, Williams MD, Howlett DC
Pleomorphic Adenoma Arising From Accessory Parotid Tissue Presenting as Dysphonia.
Journal of the Royal Army Medical Corps 2007; 154 (1): 57-59
CT “Invisible” Lesion of the Major Salivary Glands
Clinical Radiology 2009; 64 (11): 1137

Salivary Gland Mucosa – Associated Lymphoid Tissue Lymphoma in 2 Patients with Sjogren’s Syndrome: Clinical and Sonographic Features with Pathological Correlation.

A Systematic Review and Meta-Analysis of the Diagnostic Accuracy of Frozen Section for Parotid Gland Lesions.
American Journal of Clinical Pathology 2011; 136; 729-738

A Systematic Review and Meta-Analysis of the Diagnostic Accuracy of Fine Needle Aspiration Cytology for Parotid Gland Lesions.
American Journal of Clinical Pathology 2011; 136; 45-59
Diagnostic Adequacy and Accuracy of Fine Needle Aspiration Cytology in Neck Lump Assessment: Results From Regional Cancer Network Over a One Year Period.
Journal of Laryngology and Otology 2007; 121: 571-579

A Systematic Review and Meta-Analysis of the Diagnostic Accuracy of Ultrasound-Guided Core Needle Biopsy for Salivary Gland Lesions.

[21] Witt BL, Schmidt RL
Ultrasound Guided Core Needle Biopsy of Salivary Gland Lesions; A Systematic Review and Meta – Analysis.
The Laryngoscope 2014; 124: 694-700

[22] Howlett DC, Kesse KW, Hughes DV, Sallomi DF
The Role of Imaging in the Evaluation of Parotid Disease
Clinical Radiology 2002; 57; 692-701

[23] Howlett DC
High Resolution Ultrasound Assessment of the Parotid Gland
British Journal of Radiology 2003; 76:271—277
Sonographic Assessment of the Submandibular Space
Clinical Radiology 2004; 59: 1070 – 1078

Diseases of the Submandibular Gland as Demonstrated Using High
Resolution Ultrasound.

[26] Sellon E, Moody AB, Howlett DC
Ultrasound Guided Core Biopsy is the Diagnostic Tool of Choice in Salivary
Gland Swellings
British Medical Journal 2012; 345; e7782

[27] Howlett DC, Moody AB, Williams M
Fine Needle Aspiration in the Management of a Parotid Mass
The Surgeon 2006;4 (3); 185

[28] Mandalia UY, Moody AB, Howlett DC
Parotid Cancer Treatment with Surgery Followed by Radiotherapy
Annals of the Royal College of Surgeons of England 2011; 93: 561-565

[29] Bajwa J, Christodolou D, Howlett DC
Biopsy of Major Salivary Gland Masses
The Diagnostic Value of Fine Needle Aspiration in Parotid Lumps
Annals of the Royal College of Surgeons of England 2014; 93 (3): 253

[31] Brennan PA, Herd MK, Howlett DC, Gibson D, Oeppen RS
Is Ultrasound Alone Sufficient for Imaging Superficial Lobe Benign Parotid Tumours Before Surgery?

Ultrasound Guided Core Biopsy for the Diagnosis of Lumps in the Neck: Results in 82 Patients.
British Journal of Oral and Maxillofacial Surgery 2006; 44: 34-37

[33] Saha S, Woodhouse NR, Gok G, Ramesar K, Moody AB, Howlett DC
Ultrasound Guided Core Biopsy, Fine Needle Aspiration Cytology and Surgical Excision Biopsy in the Diagnosis of Metastatic Squamous Cell Carcinoma in the Head and Neck
European Journal of Radiology; 2011: 80; 792-795
[34] Burke C, Thomas R, Inglis C, Baldwin A, Ramesar K, Grace R, Howlett DC
Ultrasound Guided Core Biopsy in the Diagnosis of Lymphoma of the Head and Neck – A 9 Year Experience.
British Journal of Radiology 2011; 84: 727-732

[35] Witcher T, Williams MD, Howlett D C
“One-Stop” Clinics in the Investigation and Diagnosis of Head and Neck Lumps.

[36] Fakhry N, Santini A, Lagier N,
Fine Needle Aspiration Cytology and Frozen Section in the Diagnosis of Malignant Parotid Tumours.

[37] Olsen KD, Moore EJ, Lewis JE.
Frozen Section Pathology for Decision Making in Parotid Surgery
JAMA Otolaryngology – Head and Neck Surgery 2013; 139(12): 1275-1278
7. Appendices: Published Works and Supporting Correspondence

a) Diagnostic Ultrasound in Major Salivary Gland Assessment
   Papers 4.1 – 4.3

b) The Use of Ultrasound Guided Core Biopsy (USCB) in the Histological Diagnosis of a Major Salivary Gland Lesion
   Papers 4.4 – 4.11
7a. **Diagnostic Ultrasound in Major Salivary Gland Assessment**

4.1 Mandalia U Y, Porte F N, Howlett D C

Salivary Gland: Oncologic Imaging.

Ultrasound Clinics of North America 2014; 9; 99-113

4.2 Sriskandan N, Hannah A, Howlett D C

A Study to Evaluate the Accuracy of Ultrasound in the Diagnosis of Parotid Lumps and to Review the Sonographic Features of Parotid Lesions – Results in 220 Patients.

Clinical Radiology 2010; 65:366-372

4.3 Westerland O, Howlett D C

Sonoelastography Techniques in the Evaluation and Diagnosis of Parotid Neoplasms

European Radiology 2012; 22 (9) 66-969
7b. The Use of Ultrasound Guided Core Biopsy (USCB) in the Histological Diagnosis of a Major Salivary Gland Lesion

4.4 Buckland J R, Manjaly G, Violaris N, Howlett D C
Ultrasound Guided Cutting Needle Biopsy of the Parotid Gland
Journal of Laryngology and Otology 1999; 113; 988-992

4.5 Keese KW, Manjaly G, Violaris N, Howlett D C
Ultrasound Guided Biopsy in the Evaluation of Focal Lesions and Diffuse Swelling of the Parotid Gland.
British Journal of Oral and Maxillofacial Surgery 2002; 40; 364-368

4.6 Howlett D C
Diagnosing a Parotid Lump: Fine Needle Aspiration Cytology or Core Biopsy?

4.7 Howlett D C, Menezes LJ, Lewis K, Moody AB, Violaris N, Williams M D
Sonographically Guided Core Biopsy of a Parotid Mass
American Journal of Roentgenology 2007; 188-223-227
4.8 Breeze J, Andi A, Williams M D, Howlett D C

The Use of Fine Needle Core Biopsy Under Ultrasound Guidance in the Diagnosis of a Parotid Mass


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Diagnostic Investigation of Parotid Neoplasms – a 16 Year Experience of Freehand Fine Needle Aspiration Cytology and Ultrasound Guided Core Biopsy


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British Journal of Oral and Maxillofacial Surgery – accepted for publication August 2014
4.1 Mandalia U Y, Porte F N, Howlett D C

Salivary Gland: Oncologic Imaging. Ultrasound Clinics of North America
2014; 9:99-113
A.Mandala@brighton.ac.uk

Subject: David Howlett -PhD by publication.

Dear Anne

Re: Mandala U, Porte F N, Howlett DC


I am writing to confirm that David Howlett made a significant contribution to the above paper. David was involved with the conception and design of this review article, he supplied the images used within the article, assisted with critical revision for important intellectual content and finally approved the version to be published.

With best wishes.

Uday Mandalia

Dr Uday Mandalia MRCPCH FRCR
Salivary Gland: Oncologic Imaging

Uday Y. Mandalia, MBBS, BSc, MRCPCH, FRCP*†, François N. Porte, MBBS, FRCP*, David C. Howlett, FRCP, FRCP†

KEYWORDS
- Salivary gland • Neoplasm • Ultrasound • Ultrasound-guided biopsy

KEY POINTS
- Salivary gland neoplasms constitute a wide range of benign and malignant disorders and imaging constitutes an integral part of the initial assessment of a suspected salivary gland lesion.
- Because of their location, the salivary glands are readily accessible with high-resolution ultrasound, which is considered the first-line imaging modality in many centers.
- By providing information regarding the site, nature, and extent of disorder, ultrasound can characterize a lesion with a high degree of sensitivity and specificity.
- Ultrasound can also be used for image-guided interventions with fine-needle aspiration cytology or core biopsy.
- Ultrasound provides a guide for further imaging with computed tomography or magnetic resonance imaging as required.

ANATOMY OF THE PAROTID SPACE
The parotid gland lies in the retromandibular fossa and is bordered posteriorly by the superficial masseter muscle and the mastoid process. The masseter and medial pterygoid muscles are located anteromedial to the gland, along with the mandibular ramus. The gland consists of superficial and deep lobes, which are defined by the path of the facial nerve traveling through the gland. The superficial lobe is readily imaged with high-frequency ultrasound, although the deep lobe cannot be easily visualized in its entirety, because it is partially obscured by the mandible. The superficial lobe is also not usually identified on ultrasound; however, its position can be inferred because it passes in a plane just superficial to the adjacent retromandibular vein (RMV). Hence, identification of the RMV allows compartmentalization into superficial and deep lobes. Lying inferior to the retromandibular vein is the external carotid artery, which branches into the maxillary and superficial temporal arteries within the gland (Figs. 1 and 2).

The parotid duct, or Stensen duct, exits the gland anteriorly, passes above the masseter muscle, and perforates the buccal fat and buccinator muscle to open into the oral cavity at the level of the second upper molar. Accessory parotid tissue may be found along the course of the parotid duct, arising in approximately 20% of the population. The parotid gland is predominantly a serous gland. The parotid gland becomes encapsulated later embryologically than the submandibular and sublingual glands, and therefore intraglandular lymph nodes may be found within it. These nodes tend to be located in the preauricular portion of the gland or within the parotid tail. A normal parotid lymph node is oval or kidney shaped with a smooth contour; has a central, echo-bright fatty hilum; and contains a feeding hilar vessel that can be seen on color Doppler ultrasound.
Fig. 1. Transverse sonogram of the left parotid (A) with corresponding schematic diagram (B), showing the position of the retromandibular vein, allowing compartmentalization into superficial and deep lobes. The probe position is seen in the inset diagram.

Fig. 2. Longitudinal sonogram of the left parotid showing normal anatomy of the retromandibular vein and external carotid artery.
ANATOMY OF THE SUBMANDIBULAR GLAND

The submandibular gland lies in the space located inferior to the body of the mandible and between the anterior and posterior bellies of the digastric muscle. The gland is roughly triangular in shape and, like the parotid gland, is made up of superficial and deep lobes, although these are of less clinical significance than the parotid gland. The submandibular gland does not contain lymph nodes, although lymph nodes are found within the submandibular space superior and anterior to the gland.³

The facial artery arises from the external carotid artery and passes through a groove on the posterior aspect of the submandibular gland. The facial artery may pass through the parenchyma of the gland.³ The facial vein crosses the superficial aspect of the gland. The marginal mandibular nerve also crosses the gland superficially, within the deep cervical fascia. The submandibular duct (or Wharton duct) originates from multiple ductal branches situated on the deep aspect of the gland, extends anteriorly between the mylohyoid and hypoglossus muscles, crosses the median aspect of the sublingual gland, and drains into the mouth at the sublingual caruncle, situated on the frenulum linguae. The submandibular gland is a mixed serous/mucinous gland.

ANATOMY OF THE SUBLINGUAL GLAND

The sublingual gland is the smallest of the 3 major salivary glands. It is situated posterior to the mandible and lies below the mucous membrane of the floor of the mouth. The gland is bordered inferiorly by the mylohyoid muscle and medially by the genioglossus and the submandibular duct. The sublingual gland has a variable number of excretory ducts, many of which drain directly into the floor of the mouth, although some ducts form the sublingual duct of Bartholin, which joins the submandibular duct to drain into the sublingual caruncle. The gland can be visualized on ultrasound when scanning in the submental region and appears as an echoogenic oval-shaped structure on transverse imaging.³ The sublingual gland is a predominantly mucinous gland.

CLINICAL PRESENTATION OF A SALIVARY GLAND TUMOR

Major salivary gland tumors present as painless masses in the region of the affected salivary gland. Benign tumors are usually slow growing, whereas malignant tumors vary in their rate of growth depending on their grade, although a sudden painful increase in size may also be related to infection (Fig. 3). Pain is a poor discriminator between benign and malignant disease because it is experienced in 5.1% of patients with benign tumors and 6.5% of patients with malignant disease.⁴ However, in patients with proven salivary gland carcinoma, the presence of pain is a poor prognostic indicator, because it signifies perineural spread of disease, which is associated with a 5-year reduction in survival from 68% to 35%. Cranial nerve VII is most commonly involved because of its course through the parotid, thus symptoms include facial pain and facial nerve paralysis. With progressive tumor invasion other cranial nerves may become involved.⁵,⁶

Lymph node metastases from a salivary gland tumor may present as a firm enlarging neck lump. The primary drainage for the parotid and submandibular glands is to the deep cervical chain, whereas the sublingual gland drains to submental and submandibular nodes. Nodal metastases are associated with a poorer prognosis, with an associated reduction in 10-year survival from 63% to 33%.⁷

Distant metastasis is also an indicator of poor prognosis and is seen in 20% of the parotid cancers, most commonly from adenoid cystic carcinoma, followed by undifferentiated carcinoma.⁸

THE ROLE OF IMAGING

The diagnosis of a salivary gland tumor ideally is based on the concept of triple assessment:

1. Clinical evaluation
2. Imaging
3. Histologic/cytologic evaluation

Although salivary gland tumors are rare and usually benign, surgical excision represents the
Treatment of choice in most circumstances. Imaging is needed not only to confirm the presence of a lesion but also to determine its spread, intraglandular/extraglandular extent, identification of clinically occult lesions, as well as unsuspected cervical lymphadenopathy. The imaging characteristics of a lesion can determine whether a tumor is benign or malignant with a high sensitivity and specificity. An accurate preoperative diagnosis of a parotid lesion is critical because many non-neoplastic lesions do not require surgery. The need for surgery may also be avoided in certain benign neoplasms (e.g., Warthin tumors) if the patient is considered too elderly or unfit for surgery. An accurate preoperative diagnosis is an important determinant for operative planning, notably with the increased use of extracapsular, parotid-sparing dissection and to allow appropriate informed patient consent (in particular pertaining to facial nerve integrity and also possible nodal dissection in malignancies). Ultrasound is frequently accepted as the initial imaging modality of choice. It has the advantages of being portable and allowing multiplanar, non-invasive imaging without the need of ionizing radiation. High-frequency linear array probes are capable of producing high-resolution images of the salivary glands with a spatial resolution surpassing computed tomography (CT) and magnetic resonance (MR) imaging. However, compared with these modalities, ultrasound has some disadvantages: it is operator dependent and is limited in visualization of large lesions or those extending into the deep lobe of the parotid because of obscuration by the mandible.

Most lesions lie within the superficial lobe and ultrasound is usually able to compartmentalize a lesion according to its relationship to intraparotid vessels and the inferred position of the facial nerve. For large or suspected malignant lesions and lesions of the deep lobe of the parotid gland, MR imaging or CT are the modalities of choice; however, even in these cases, ultrasound can act as an indicator for additional investigation.

Following the initial sonographic diagnosis of a salivary gland tumor, ultrasound-guided biopsy (with fine-needle aspiration cytology [FNAC] or ultrasound-guided core biopsy [USCB]; discussed later) is a safe and reliable method of obtaining the histopathologic confirmation of a lesion necessary to institute further surgical management. The goals of imaging salivary gland tumors can be seen in Box 1.

### SONOGRAPHIC TECHNIQUE

A high-frequency linear array transducer, typically 7 to 12 MHz or greater, should be used in the assessment of the salivary glands. A lower frequency transducer (5–10 MHz) can be used to assess large tumors fully and to visualize lesions located in the deeper aspects of the glands.

To facilitate visualization, a pillow or towel can placed under the patient's shoulders to extend the patient's neck. The salivary glands and any lesion discovered within them should be interrogated in at least 2 perpendicular planes. An oblique approach may be required to navigate around the mandible. The contralateral salivary gland needs to be examined for comparison and to look for bilateral disease. To complete the study, the entire neck should be imaged for related disorders and lymph node enlargement. Color Doppler assessment provides information regarding the vascular resistance and flow pattern of a lesion, which can improve diagnostic accuracy for malignant tumors.

### SALIVARY GLAND NEOPLASTIC DISEASE

When all salivary gland tumors are considered, the global incidence varies from 0.4 to 13.5 cases per 100,000 population. About 80% of all lesions are benign. Hence, salivary malignancies are rare entities, comprising less than 0.6% of all malignancies and about 5% of cancers of the head and neck. They constitute a wide variety of disorders (Table 1). They are divided into benign and malignant neoplasms, which can be epithelial or nonepithelial in origin. The parotid gland contains 70% of all salivary gland tumors, with 83% found in the submandibular glands and 22% in the minor glands.

There are some general rules that apply to salivary gland neoplasms. The smaller the salivary gland, the higher the rate of malignancy. Thus, the rate of malignancy increases from 20% to 25% in the parotid gland to 40% to 50% in the submandibular gland, and to 50% to 81% in the sublingual glands and minor salivary glands. Environmental and genetic factors have been proposed as causes of salivary gland neoplasms. The strongest link seems to be with radiation exposure and smoking, which have been implicated in the development of Warthin tumors.
<table>
<thead>
<tr>
<th>Table 1</th>
<th>World Health Organization classification of epithelial salivary gland neoplasms</th>
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<tr>
<td>Benign Epithelial Tumors</td>
<td>Malignant Epithelial Tumors</td>
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<tr>
<td>Pleomorphic adenoma</td>
<td>Acinic cell carcinoma</td>
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<tr>
<td>Myoepithelioma</td>
<td>Mucoepidermoid carcinoma</td>
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<tr>
<td>Basal cell adenoma</td>
<td>Adenoid cystic carcinoma</td>
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<tr>
<td>Warthin tumor</td>
<td>Polymorphous low-grade adenocarcinoma</td>
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<tr>
<td>Oncocytoma</td>
<td>Epithelial-myoepithelial carcinoma</td>
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<tr>
<td>Canalicul ar adenoma</td>
<td>Clear cell carcinoma, not otherwise specified</td>
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<tr>
<td>Sebaceous adenoma</td>
<td>Basal cell adenocarcinoma</td>
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<td>Sebaceous adenoma</td>
<td>Sebaceous carcinoma</td>
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<td>Sebaceous nonsebaceous ductal papilloma</td>
<td>Sebaceous lymphadenocarcinoma</td>
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<td>Inverted ductal papilloma</td>
<td>Cystadenocarcinoma</td>
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<td>Muscosus adenocarcinoma</td>
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<td>Cystadenoma</td>
<td>Oncocytic carcinoma</td>
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<tr>
<td>Salivary duct carcinoma</td>
<td>Adenocarcinoma not otherwise specified</td>
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<tr>
<td>Myoepithelial carcinoma</td>
<td>Carcinoma ex pleomorphic adenoma</td>
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<tr>
<td>Carcinoma</td>
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<td>Lymphoepithelial carcinoma</td>
<td>Lymphoblastoma</td>
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<td>Diffuse large B-cell lymphoma</td>
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<td>Hemangioma</td>
<td>Extramedullary marginal zone B-cell lymphoma</td>
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<tr>
<td>Hematolymphoid tumors</td>
<td>Secondary tumors</td>
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**BENIGN TUMORS**

About 68% of all salivary gland tumors are pleomorphic adenomas, followed by Warthin tumor in 3.9% to 5.0% depending on geographic location. The remainder are rare benign tumors.23 On ultrasound these lesions typically appear as smooth, round, hypoechoic masses with distal acoustic enhancement (Fig. 4). These tumors may appear lobulated. Large tumors may appear more heterogeneous than small ones and may require further evaluation with MRI imaging.

**PLEOMORPHIC ADENOMAS**

Pleomorphic adenomas represent the most common benign parotid and submandibular tumor. They are of mixed cell origin with considerable variation in the myoepithelial, mesenchymal, and epithelial components. They usually present as slow-growing, asymptomatic masses in middle-aged patients. Pleomorphic adenomas occur most often in people in the fourth and fifth decades of life but may arise at any age. They have a slight female preponderance. About 80% of pleomorphic adenomas arise in the parotid; 10% in the submandibular gland; and 10% in the minor salivary glands of the oral cavity, nasal cavity, and paranasal sinuses and the upper respiratory and alimentary tracts.24 Of the parotid lesions, 90% occur in the superficial lobe, frequently in the tail. They are usually solitary and unilateral.25,31

If left untreated, approximately 5% undergo malignant transformation, usually after a period of decades.3,76 In view of their malignant potential, surgical resection is the mainstay of treatment. Pleomorphic adenomas treated by surgical enucleation or those that experience intraoperative rupture or transaction have a high rate of multifocal local recurrence, and they can rarely behave aggressively, showing metastatic spread.36
On ultrasound, pleomorphic adenomas are characteristically hypoechoic, well-defined, lobulated tumors with posterior acoustic enhancement (see Fig. 4). Larger tumors may appear poorly defined with cystic degeneration and internal heterogeneity and can be mistaken for malignancy (Fig. 5). Multifocal primary lesions have also been reported. The homogeneity of internal echoes has been regarded as a typical feature of pleomorphic adenoma; however, it is likely to depend on tumor composition. Dystrophic calcifications may also form in long-standing lesions and are best visualized with CT.

**WARLHN TUMOR (CYSTADENOLYMPHOMA)**

Warthin tumor is the second most common benign neoplasm of the salivary gland. It is exclusively found in the parotid and accounts for 20% of all epithelial parotid tumors. It arises from heterotopic parotid tissue within parotid lymph nodes. These tumors present as slow-growing masses within the superficial lobe of the parotid near the angle of the mandible. They are most commonly found in elderly men in the fifth to sixth decade and are associated with smoking and ionizing radiation. Warthin tumors can be bilateral or multiple in 15% of patients. Tumors are melechronous in 75% of multifocal cases.

On sonography, these tumors are rounded or lobulated hypoechoic masses that may show cystic change with hyperechoic internal septation. They may present as entirely cystic structures, requiring differentiation from other benign and malignant cystic lesions (Figs. 6–8). Biopsy of these tumors can be challenging because of the paucity of solid material; however, core biopsies through the tumor wall may allow histologic diagnosis.

On MRI imaging these tumors are homogenous to intermediate signal on T1. On T2-weighted imaging they are intermediate signal with focal hyperintense areas corresponding with cystic components. A characteristic feature of Warthin tumors is their lack of enhancement with gadolinium. Warthin tumors show increased tracer uptake on 99mTc scintigraphy.

![Warthin tumor (calipers) of the right parotid. Note the inhomogeneous internal architecture and cystic changes.](image)
ONOCYTOMA

Oncocytoma is an uncommon, benign salivary neoplasm composed of mitochondria-rich epithelial cells called oncocyes. They account for about 1% of all the salivary gland neoplasms. Most (84%) cases occur in the parotid gland, with the remainder occurring in the submandibular and minor glands. They present as slow-growing, painless, mobile masses usually within the superficial lobe of the gland.

Oncocytoma has similar imaging characteristics to pleomorphic adenoma. On ultrasound these lesions appear well circumscribed and lobulated. Lesions may present at any age but two-thirds of cases are diagnosed in the first 2 decades. They are the most common type of pediatric salivary gland tumor arising in infancy and undergo involution usually by the age of 9 years. They are twice as common in female patients as in male patients.

Hemangiomas of the parotid appear solid and hypoechoic on ultrasound. On color Doppler imaging they show prominent internal vascularity. Calcified phleboliths are commonly seen within these tumors.

Lipomas of the salivary glands are rare; however, they can occur in the parotid and account for approximately 1% to 2% of all parotid neoplasms. On sonography the lesions are usually well-defined but can also appear ill-defined. They are normally hypoechoic and contain internal echogenic foci or striations.

OTHER BENIGN NONEPITHELIAL TUMORS

Hemangiomas of the salivary glands account for approximately 0.4% of salivary tumors. Lesions may present at any age but two-thirds of cases are diagnosed in the first 2 decades. They are the most common type of pediatric salivary gland tumor arising in infancy and undergo involution usually by the age of 9 years. They are twice as common in female patients as in male patients.

Hemangiomas of the parotid appear solid and hypoechoic on ultrasound. On color Doppler imaging they show prominent internal vascularity. Calcified phleboliths are commonly seen within these tumors.

Lipomas of the salivary glands are rare; however, they can occur in the parotid and account for approximately 1% to 2% of all parotid neoplasms. On sonography the lesions are usually well-defined but can also appear ill-defined. They are normally hypoechoic and contain internal echogenic foci or striations.

MALIGNANT LESION

Sonographic features that suggest a malignant lesion are ill-defined borders, hypoechoic and heterogeneous architecture with distal acoustic shadowing, and extraglandular extension (Figs. 10–12).

MUCOEPIDERMOID CARCINOMA

Mucocoeplidermoid carcinoma is the most common primary malignancy of the salivary glands, representing 20% of all salivary gland malignancies. They arise from ductal epithelium. Approximately half of tumors (63%) occur in major glands, most frequently in the parotid gland, representing 45%, with 7% in the submandibular glands, and 1% in sublingual glands. The most frequent intranodal sites are the palate and buccal mucosa. Lesions tend to occur in middle-aged adults (35–65 years). Sonographic features depend on the histologic grade of the tumor. Most tumors
are low to intermediate grade, and have a good prognosis with surgery. However, high-grade tumors have a poorer prognosis and increased metastatic potential.22

Lower grade lesions appear well defined and may display a lobulated shape with homogenous internal architecture, displaying significant overlap with pleomorphic adenomas both sonographically and clinically (Fig. 13). High-grade aggressive lesions are poorly defined, with an irregular shape; blurred margin; and hypoechoic, heterogeneous internal architecture (Fig. 14). Tumors may be predominantly cystic or mixed cystic with solid mural components.23,35,50 Once biopsy has confirmed diagnosis, MR imaging is necessary to complete locoregional staging and a CT of the chest to look for metastatic spread.

ADENOID CYSTIC CARCINOMA

Adenoid cystic carcinoma is the second most common parotid malignancy. It accounts for 2% to 6% of parotid gland tumors and is the most common submandibular and minor salivary gland malignancy.26

The tumor presents as a painful slow-growing mass. The tumor is unencapsulated and may appear well circumscribed on ultrasound. These tumors have a tendency for perineural and local invasion, which explains the high incidence of associated facial pain (33%) and facial nerve paralysis. Late recurrence can occur up to 20 years after treatment. Perineural invasion can be accurately assessed with multiplanar MR imaging and abnormal neural enhancement and skull base extension may be seen after contrast.47,61

METASTASIS

The parotid gland contains lymphatic tissues and lymph nodes because of its late encapsulation, within which metastatic disease may occur. Metastatic spread is most commonly via the scalp lymphatics with squamous carcinoma (37%) and
LYMPHOMA

Primary salivary gland lymphoma is rare, accounting for only 5% of all primary extranodal lymphomas and 2% of all salivary gland tumors.\(^{59}\)

The most commonly affected gland is the parotid gland (75%), followed by the submandibular gland (20%). Most lymphomas occurring in salivary glands are mucosa-associated lymphoid tissue (MALT) lymphomas, which are low-grade B-cell non-Hodgkin lymphomas (NHL), that often develop in the setting of chronic lymphoepithelial sialadenitis seen in patients with Sjögren syndrome (Figs. 16 and 17).\(^{57,58}\) Primary and secondary non-MALT lymphomas of the salivary glands may also occur and involvement can be in the form of focal nodal disease or diffuse infiltration of the gland.\(^{59}\)

The imaging features of parotid lymphoma are variable. Focal lymphomatous nodes may have a pseudocystic or micronodular pattern (Fig. 18), whereas diffuse involvement may present as generalized enlargement of the gland. There may be associated regional lymphadenopathy and glandular sialectasis. Diffuse disease may manifest with a pattern of multiple hypoechoic lesions with increased vascularity. In these circumstances, differentiation from benign inflammatory conditions is required.\(^{59,61}\)

CARCINOMA EX PLEOMORPHIC ADENOMAS

There are 3 types of malignancies that occur within preexisting pleomorphic adenomas. The most common is the carcinoma ex pleomorphic adenoma, which originates from epithelial cells; these represent 12% of all malignant salivary gland tumors. The other two forms are true malignant mixed tumor (carcinosarcoma) and metastasizing pleomorphic adenoma.\(^{60,62}\) Concerning features of malignant degeneration are pain and a sudden increase in size within a long-standing mass. However, this is also seen in tumor infarction (see Fig. 3). The rate of occurrence increases with the period the pleomorphic adenoma is left untreated. According to some investigators, the rate of malignant change is 1.5% in the first year in which the adenoma goes untreated, and increases to 9.5% after 15 years.\(^{64,65}\)

On imaging they look similar to a pleomorphic adenoma, or may show infiltrative margins, necrotic areas, and regional lymph node involvement.

COLOR FLOW ASSESSMENT

Malignant lesions tend to show increased, disordered, and chaotic vascularity compared with benign lesion. Various studies have used different markers of vascularity to differentiate between benign and malignant salivary gland tumors. Some studies have shown that highly vascular lesions and those with a high systolic peak flow velocity (>25 cm/s) are suspicious of malignancy.
regardless of the gray-scale appearance of the tumor. However, measurement of peak systolic velocity in small intratumoral vessels is imprecise, and doubts have been raised regarding the ability to accurately angle correct on small intratumoral vessels.\textsuperscript{56,57}

Other studies have measured the vascular resistance of intratumoral vessels, showing that tumors with an increased resistance have an increased risk of malignancy. In those with high pulsatility index (PI) and resistive index (RI), the risk of malignancy increases by a third (PI>1.8 and RI>0.8).\textsuperscript{31}

TUMOR MIMICS

Pseudotumors are mimics of salivary gland tumors. Lymphadenopathy in the region of the salivary glands can be misinterpreted as a mass of salivary gland origin. This mass may be secondary to inflammatory conditions such as sarcoid or nodal metastases from head and neck cancers (Fig. 19).

Another important example is the Kuttner tumor, a form of chronic sclerosing sialadenitis, presenting as a firm, painful swelling of 1 or both submandibular glands. The disorder is characterized by plasmacytic and lymphohistiocytic periductal infiltrates, which eventually lead to encasement of ducts with fibrotic tissue.\textsuperscript{58} On ultrasound, the gland appears diffusely hypoechoic and heterogeneous with multiple small hypoechoic foci with background heterogeneity. Features have been likened to the appearance of a cirrhotic liver. On color Doppler, affected glands showed prominent vascularity.\textsuperscript{59} The sonographic appearances are typical and biopsy confirmation is often not required (Fig. 20).
PITFALLS

Ultrasound is able to determine whether a lesion is malignant with a high sensitivity and specificity of approximately 90%.

However, as discussed earlier, there is overlap in characteristics of malignant and benign tumors and distinguishing between the various lesions based on ultrasound criteria alone is not always possible. Therefore, in most patients, ultrasound acts as a guide for further investigation, usually with biopsy in the first instance.

INTERVENTIONAL SALIVARY GLAND ULTRASOUND

Open surgical excision biopsy (SEB), as a method of obtaining a histologic sample, has long fallen out of favor because of the risk of tumor seeding, facial nerve injury, facial scarring, and fistula formation. The accuracy of frozen section diagnoses of the salivary gland is also controversial, with suboptimal accuracy rates for malignancy.

Nonsurgical approaches to tissue diagnosis, particularly FNAC, have therefore been widely adopted. FNAC is a rapid and safe sampling technique that can readily be performed in the outpatient setting using ultrasound guidance. With a skilled operator and on-site histopathologist backup and the latest laboratory techniques, FNAC has a high diagnostic accuracy. However, these services are expensive and not widely available outside large and specialist centers. A recent meta-analysis of FNAC based on 64 studies concluded that FNAC had a sensitivity of 0.79 for a diagnosis of malignancy. In addition to the high false-negative rate for malignancy, the study also highlighted the significant heterogeneity in the performance of FNAC, making it impossible to provide a general guideline for its clinical usefulness.

In general, FNAC is capable of a high specificity, in optimized circumstances, but has a lower sensitivity for the detection of malignancy, thus the false-negative plus high nondiagnostic rates of FNAC are disadvantages.

USCB has recently been described in the diagnosis of parotid tumors, and is developing into an established technique. Because USCB provides a larger sample, it potentially has a lower nondiagnostic rate, providing diagnostic biopsies without the need for on-site cytology. The core of tissue provided by USCB can also be used for immunohistochemical analysis, which can help
with the grading and typing of parotid malignancy that is crucial in diagnosis of lymphomas. Several studies on the performance of USCB have shown the good diagnostic yields from USCB of the salivary glands.\textsuperscript{75,76} A recent meta-analysis of 6 studies compiled in 2011, evaluating the accuracy of USCB in the diagnosis of salivary gland lesions, concluded that choice of the test (FNAC vs USCB) to use for an individual patient remains undefined; however, the overall accuracy of core needle biopsy is greater than FNAC in some practice settings, with less variability in performance.\textsuperscript{30}

**NEW DEVELOPMENTS**

Sonoclastography is a novel imaging technique that can map the elastic properties of soft tissues.\textsuperscript{63} A mechanical force, usually manual compression via the ultrasound probe, is applied to the region of interest. The degree and distribution of tissue deformation is detected and characterized sonographically, and is represented visually as an elastogram of the area of interest. The technique is performed using a 5-MHz to 12-MHz linear array transducer and requires a compatible ultrasound machine. Shear wave elastography (SWE) is a variation of sonoclastography.\textsuperscript{32} In SWE, instead of the compressive force of the transducer probe the applied mechanical force consists of focused pulses of ultrasound waves termed push pulses. These induce shear waves that are detected by an ultrafast ultrasound imaging technique. This technique is thought to be more accurate than strain elastography because it produces quantitative estimates of stiffness and is less operator dependent. There have been several studies of the ability of sonoclastography to differentiate parotid neoplasms. These studies have been limited.
by small patient cohorts and interoperator variability, and the initial results have been disappointing. Recent work focusing on identifying characteristic elastographic patterns within benign and malignant parotid lesions has shown potential in improving preoperative lesion characterization; however, biopsy is likely to remain necessary in the near future.

WHAT THE REFERRING CLINICIAN NEEDS TO KNOW

Ultrasound is the initial imaging investigation of choice in virtually all parotid and submandibular gland masses and has a high specificity and sensitivity when differentiating benign from malignant tumors.

Ultrasound-guided biopsy of salivary lesions is a safe, rapid, and accurate method of obtaining tissue samples for analysis. Ultrasound can obviate further imaging if a lesion is sonographically confined to the superficial lobe and confirmed as benign on biopsy.

MR imaging is recommended in the imaging of deep parotid lesions or suspected malignant tumors, for which further assessment of local invasion and perineural spread is required. CT is a useful adjunct for assessing bony involvement and staging tumors in malignancy.

SUMMARY

Salivary gland neoplasms constitute a wide range of benign and malignant disorders and imaging constitutes an integral part of the initial assessment of a suspected salivary gland lesion. Because of their location, the salivary glands are readily accessible with high-resolution ultrasound, which is considered the first-line imaging modality within many centers. By providing information regarding the site, nature, and extent of a disorder, ultrasound can characterize a lesion with a high degree of sensitivity and specificity. Ultrasound can also be used for image-guided intervention with FNAC or core biopsy. It provides a guide if further CT or MR imaging are required.

REFERENCES


4.2 Sriskandan N, Hannah A, Howlett D C

A Study to Evaluate the Accuracy of Ultrasound in the Diagnosis of Parotid Lumps and to Review the Sonographic Features of Parotid Lesions: Results in 220 Patients.

Clinical Radiology 2010; 65:366-372
A.Mandy@brighton.ac.uk

Subject: David Howlett PhD Publication

Dear Anne

Re: Sriskandan N, Hannah A, Howlett DC

A study to evaluate the accuracy of ultrasound in the diagnosis of parotid lumps and to review the sonographic features of parotid lesions – results in 220 patients.


I am writing to confirm that David Howlett made a significant contribution to the above paper. He was largely responsible for study conception, design and data acquisition, he also assisted with data analysis and interpretation. He critically revised the paper for important intellectual content and was involved in final approval of the version to be published.

Furthermore, the above paper was also awarded the Ellis Barnett Prize by the Royal College of Radiologists in 2010 for the most outstanding paper with an ultrasound content published in Clinical Radiology.

With best wishes,

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A study to evaluate the accuracy of ultrasound in the 
diagnosis of parotid lumps and to review the sonographic 
features of parotid lesions — results in 220 patients

N. Sriskandan*, A. Hannah, D.C. Howlett

Department of Radiology, Eastbourne District General Hospital, Eastbourne, East Sussex, UK

AIM: To assess the accuracy of ultrasound in characterizing benign and malignant parotid lesions and to review their sonographic features.

MATERIALS AND METHODS: A retrospective analysis of 220 ultrasound examinations was undertaken in 220 patients who presented with palpable parotid lumps over an 11-year period and correlated with the clinic-histopathological findings. The original sonographic diagnosis was compared to the final histopathology and lesions characterized using previously established sonographic criteria.

RESULTS: Histopathology results were available for all patients. Two hundred and two patients had local lesions: 29 carcinomas, 21 lymphomas and 153 benign lesions (including 62 pleomorphic adenomas and 54 Warthin’s tumours). Ten patients did not have local lesions. The initial ultrasound report was indeterminate in 25/201 local lesions. In the remaining 176 lesions, the sensitivity, specificity, and diagnostic accuracy for malignancy of ultrasound was 94%, 90%, and 93%, respectively. There were four false-negative and nine false-positive with a crossover of apparently benign and malignant features. Pleomorphic adenomas and Warthin’s tumours were poorly differentiated using ultrasound. Additional impalpable parotid lesions or adenopathy were detected in 44 patients using ultrasound.

CONCLUSION: Ultrasound is a valuable adjunct to clinical examination, accurately differentiating benign from malignant lesions and diagnosing non-local diseases. There is an overlap in features of pleomorphic adenomas and Warthin’s tumours and of some benign and malignant lesions. Diagnostic ultrasound should be combined with needle biopsy in most patients to maximize diagnostic yield.

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Introduction

The parotid gland is a superficial structure and readily amenable to high-resolution ultrasonography. This imaging method has become an integral part of the assessment of palpable parotid lesions that are often difficult to diagnose on clinical grounds alone. In addition to clinical assessment and diagnostic ultrasound, fine-needle aspiration cytology (FNAC) and, more recently, ultrasound-guided core biopsies (USCB) are often performed in order to obtain a histological diagnosis with high levels of diagnostic accuracy.1 Appropriate surgical management and planning, as well as patient informed consent are dependent on an accurate preoperative diagnosis.

The ability to reliably characterize parotid lesions using ultrasound alone may reduce the need for biopsy in some
patients and guide the need for further imaging and biopsy in others. Accurate preoperative imaging could potentially enable certain patients with likely benign lesions to be monitored, for example, in the elderly or those for whom surgery or biopsy carries a high risk.

There are few studies describing the sonographic features of a range of benign and malignant parotid diseases, the largest of which comprises 86 patients. Furthermore, only one study of 88 patients assessed the operator's ability to diagnose parotid lesions sonographically. The aims of the present study were to: (1) assess the accuracy of ultrasound according to original operator diagnosis when compared to final histology; (2) review the sonographic appearances of focal parotid lesions, with particular attention to the features occurring in both benign and malignant conditions; and (3) to clarify the role of ultrasound in the diagnosis of parotid lesions.

Materials and methods

A retrospective analysis was performed of consecutive parotid ultrasound examinations and reports from a single institution over an 11 year period (1997-2008). The majority of the patients were referred from the Ear, Nose, and Throat, Maxillofacial, Oncology, Haematology, or Rheumatology clinics. All the patients had been referred for diagnostic ultrasound with a view to needle biopsy of a palpable parotid lump and all had initial diagnostic ultrasound and either cytological or histological confirmation of their diagnosis with FNAC or USSC, respectively. A proportion of patients also had surgical histology following lesion excision. Patients with parotid masses who had not been referred for ultrasound imaging or in whom ultrasound-guided biopsy was not undertaken were not included in the study. The ultrasound examinations were performed and reported by the same operator using a high-frequency linear array transducer: Advanced Technology Laboratories (ATL) High Definition Imaging 3D000 ultrasound machine with a 5-10 MHz linear array transducer was used for the initial 5 year period and ATL 5000 with a 7-12 MHz linear array transducer was used for the remaining period (ATL HDI, Seattle Washington, USA; subsequently ATL HDI Philips, Amsterdam, Netherlands).

The study was performed in two stages: first, patient records were obtained and reviewed in conjunction with the ultrasound images, examination and pathology reports. The original reported ultrasound-based diagnosis had been made in conjunction with the patient's clinical history and examination, with lesions either classified as benign, malignant, or indeterminate, or where possible a specific diagnosis was made. Second, with the pathological diagnosis known, lesions were then retrospectively characterized according to their sonographic appearances using previously described sonographic criteria. Features considered consistent with pleomorphic adenomas were: well defined, homogeneous, hypoechoic with posterior acoustic enhancement; non-lymphomatous malignancies were poorly defined, hypoechoic, and heterogeneous with distal acoustic shadowing; lymphomatous lesions could range from an irregular, heterogeneous mass to multiple, small hypoechoic nodules. An attempt was also made to evaluate the colour: Doppler characterization based upon patterns of internal vascularity, resistive, and pulsatility indices. However, differentiation of primary and secondary non-lymphomatous malignancies was not attempted.

In the assessment of lymph nodes, established diagnostic criteria were again used: poorly defined borders, low echogenicity, rounded shape, loss or displacement of the echogenic hilum, chaotic peripheral vascularity, and cystic necrosis, were all considered to be features of malignancy.

Criteria for the sonographic features of parotid lesions and lymph nodes from previous studies were adopted to characterize the lesions, as shown in Table 1.

The ultrasound findings and report were compared with the final pathology report. Surgical histological diagnosis, where obtained, was taken as the final pathology diagnosis and also correlated with core biopsy or FNAC results. The final pathological diagnosis was also compared with the ultrasound characteristics to determine which features were associated with certain lesions.

Results

A total of 220 ultrasound examinations were performed on 220 patients who had presented with palpable parotid masses (122 male; 98 female; mean age 53.7 years, age range 16-87.1 years). All patients had subsequent

Table 1 Criteria for the assessment of sonographic features of parotid and lymph node lesions

| The presence of a focal lesion: |
| Stage: |
| Definition of borders: |
| grade 0 - well defined; grade 1-1/2 of border poorly defined; grade 2 - 1/3-2/3 poorly defined; grade 3 - 2/3 poorly defined |
| Hypoechoicity: |
| grade 0 - hyperechoic; grade 1-1/2 hyperechoic; grade 2 - 1/3-2/3 hyperechoic; grade 3 - 2/3 hyperechoic |
| Homogeneity: |
| grade 0 - homogeneous; grade 1-1/2 heterogeneous; grade 2 - 1/3-2/3 heterogeneous; grade 3 - 2/3 heterogeneous |
| Internal architecture: |
| absent; present; raised |
| Acoustic shadowing: |
| absent; present; raised |
| Vascularity: |
| absent; borderline; malignant; indeterminate |
| Balanced or multilobular lesions: |
| Single or multiple lesions (within the same quadrant) |
| Ultrasound and cervical lymphadenopathy: |
| benign; indeterminate; malignant |
Tissue sampling. A total of 201 patients had one or more focal lesions and 19 had no focal lesion (Table 2). These lesions were wholly or in part within the superficial lobes of the parotid. Pathological diagnosis was available for all 220 patients: USCB was performed in 214, FNAC in six, and subsequent surgical excision was performed in 124 patients, which provided the final histological diagnosis in these cases. In the surgical group of 124 patients, all underwent initial USCB with all samples suitable for histological assessment. There were no false-positive USCB results and only one false-negative result, which occurred in a well-differentiated basal cell adenocarcinoma where the lesion capsule had not been sampled and USCB had suggested an adenoma.

The frequency of ultrasound features seen in benign and malignant neoplasms are shown in Table 3. According to the original operator-based monographic diagnosis of malignancy, there were 39 true-positive, 24 true-negative, nine false-positive, and four false-negative diagnoses (Table 4). Excluding the lesions that were reported as indeterminate in appearance (n = 25), the ability of ultrasound alone to differentiate malignant from benign lesions had a sensitivity of 91.2% (95% CI: 78–97%) and a specificity of 93% (95% CI: 88–97%). The diagnostic accuracy in determining malignancy was 93% for both benign and malignant lesions.

The majority of benign and malignant lesions were unilateral and hypochogenic and contained no calcification. A poorly defined lesion had a sensitivity of 80% (95% CI: 66–90%) and a specificity of 92% (95% CI: 86–96%) for malignancy. A heterogeneous lesion had a sensitivity of 74% (95% CI: 60–88%) and a specificity of 61% (95% CI: 52–70%). Distal acoustic shadowing alone had a sensitivity of 66% (95% CI: 51–79%) and a specificity of 80% (95% CI: 82–94%) for malignancy. False-negative lesions did not have any of the described features of malignancy (Fig. 1). Whereas, the

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Frequency of cases based on final histopathological diagnosis</th>
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<tbody>
<tr>
<td>Diagnosis</td>
<td>Number of cases</td>
</tr>
<tr>
<td>Benign neoplasms</td>
<td>127</td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>77</td>
</tr>
<tr>
<td>Warthin's tumor</td>
<td>54</td>
</tr>
<tr>
<td>Lipoma</td>
<td>1</td>
</tr>
<tr>
<td>Other benign focal lesions</td>
<td></td>
</tr>
<tr>
<td>Cysts</td>
<td>10</td>
</tr>
<tr>
<td>Lymphoepithelial lesions</td>
<td>2</td>
</tr>
<tr>
<td>Glandular lesions</td>
<td>6</td>
</tr>
<tr>
<td>Reactive lymph node</td>
<td>9</td>
</tr>
<tr>
<td>Abscess</td>
<td>1</td>
</tr>
<tr>
<td>Vascular malformation</td>
<td>1</td>
</tr>
<tr>
<td>Retinal</td>
<td>1</td>
</tr>
<tr>
<td>Other benign non-focal lesions</td>
<td>9</td>
</tr>
<tr>
<td>Polygangliate</td>
<td></td>
</tr>
<tr>
<td>Auto and chronic sialadenitis</td>
<td>8</td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
</tr>
<tr>
<td>Malignant lesions</td>
<td>74</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>9</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>25</td>
</tr>
<tr>
<td>Metastasis</td>
<td>18</td>
</tr>
</tbody>
</table>

false-positive lesions had features suggestive of malignancy, including poor definition, heterogeneity, and posterior acoustic shadowing (Figs. 2 and 3).

The majority of the pleomorphic adenomas had typical features. However, cystic changes and multifocality were also seen, features considered more typical of a Warthin's tumor (Fig. 4). Cystic components and sepsis enabled the
correct diagnosis of Warthin's tumours to be made in most cases. Septa had a specificity of 97% (95% CI: 88–99%) for Warthin's tumour but a low sensitivity of 31%. Cystic changes were also more specific for Warthin's tumours at 76% (95% CI: 66–84%) but had a lower sensitivity of 61% (95% CI: 47–74%). However, in 12 cases of Warthin's tumours these features were absent and the homogeneous, hypoechoic appearance resulted in incorrect diagnoses of pleomorphic adenomas (Fig. 5). The only lipoma in our series was well defined with internal hypoechoic linear striations and posterior acoustic enhancement.

The malignant lesions that were correctly diagnosed had some of the expected features. However, distal acoustic enhancement was seen in a third of non-lymphomatous malignancies and half of lymphomas. Cystic changes had 95% specificity (95% CI: 74–100%) for non-lymphomatous malignancy compared with lymphomatous malignancy, but a low sensitivity of 52%. Four patients had a new diagnosis of Sjögren's syndrome made following initial diagnostic ultrasound assessment, with associated secondary muco-associates lymphoid tissue lymphoma (MALT). In one case the MALT lymphoma was non-palpable and an incidental finding on ultrasound that was being performed for a more superficial palpable lesion (a sebaceous cyst; Fig. 6).

Overall, it was not possible to differentiate primary from secondary non-lymphomatous malignancy, except in those patients with Sjögren's syndrome, where underlying glandular changes suggested the diagnosis.

There were a total of 27 focal, non-neoplastic lesions composed predominantly of cysts, reactive lymph nodes, and granulomatous disease. The appearances of the former two are well established.831 One lymph node was thought to be malignant due to a displaced hilum and apparently eccentric cortex but histology demonstrated reactive hyperplasia only. The granulomatous lesions were hypoechoic with varying degrees of definition and homogeneity. All these lesions contained calcification, leading to posterior acoustic shadowing in a third of cases.

Of the remaining focal, non-neoplastic lesions, the abscess was a solitary, heterogeneous lesion containing fluid and debris with moderately ill-defined borders and posterior acoustic enhancement; the vascular malformation was lobular, moderately well-delineated and homogeneous with posterior acoustic enhancement but no colour flow was demonstrated; the keloid scar was oval, well defined and heterogeneous with mixed posterior acoustic enhancement and shadowing.

There were a total of 18 non-focal lesions: nine cases of diffuse fatty infiltration, which were correctly diagnosed on ultrasound by their diffusely coarse, hypechoic appearance; a further two cases returned normal parotid tissue on histology. The sonographic appearances of the eight cases of acute and chronic sialadenitis were varied, including hypechoic and septate. However, the reported ultrasound diagnosis was correct in seven cases and indeterminate in one.

Forty-four cases of multifocal disease were detected using ultrasound examination, including 21 cases of
Warthin's tumours, five of which were bilateral; five cases of multifocal pleomorphic adenomas (confirmed histologically, see discussion); five cases of multifocal non-lymphomatous malignancies; and six cases of bilateral lymphoma. Clinical examination was only able to detect a solitary lesion in all cases. In 10 cases of malignant parotid lesions malignant adenopathy was identified at ultrasound, which had not been detected clinically. None of the patients with lymphoma underwent surgical biopsy or excision of the associated lymph nodes.

Discussion

There are few papers that describe the sonographic appearances of parotid lesions, and likewise, the direct correlation of ultrasound features with histological diagnosis is not well described. The results of the present study indicated that benign lesions are most commonly well defined and homogeneous, as previously described, and conversely, malignant lesions are poorly defined and heterogeneous. Low-grade, well-differentiated macroepidermoid carcinomas may have features very similar to pleomorphic adenomas, as shown in one false-negative diagnosis. The presence of several benign features poses a diagnostic difficulty in the reliable differentiation of benign from malignant diseases. For example, the malignant lesions demonstrated distal acoustic enhancement, with or without shadowing, in almost equal frequency as
The presence of a focal lesion with malignant features on a background of Sjögren’s syndrome is supportive of a diagnosis of lymphoma. Multifocal, unilateral non-lymphomatous malignant lesions occurred in metastatic disease, usually squamous cell carcinoma, whereas, bilateral disease was only seen in lymphoma. In the present study, differentiation between the different histological types of non-lymphomatous malignancies was not attempted.

Pleomorphic adenomas usually account for up to 80% of benign tumours but in the present study, the proportion of Warthin’s tumours was higher than expected and may be accounted for by the older age of our catchment population. There was crossover in the features seen commonly in pleomorphic adenomas and Warthin’s tumours. Multifocality, typically associated with Warthin’s tumours, was seen in five cases of pleomorphic adenomas; one case occurred in a patient who had a previous pleomorphic adenoma excised, thus enabling a correct ultrasound diagnosis of multifocal recurrence of the original lesion; in a second case the lesions were reported as having typical features of pleomorphic adenomas, but the multifocality prompted an incorrect ultrasound diagnosis of Warthin’s tumours; and the remaining three lesions had cystic changes and were all reported as Warthin’s tumours. There was no known history of previous pleomorphic adenomas in these four patients. Multifocal recurrence of pleomorphic adenomas is well recognized; however, multifocal primary lesions are rare with only 10 cases reported in the literature.

There was no specific feature identified that could be considered pathognomonic or strongly suggestive of either lesion, but it may be important to differentiate between the two lesions as their management can be different: Warthin’s tumours may be safely left in situ, particularly in the elderly, and infirm. A combination of benign characteristics with septa/cystic change and multifocality may allow a presumptive diagnosis of Warthin’s tumour.

Vascularity and formal pulsatile and resistive indices were not consistently assessed in the present study group, and due to the technical limitations of the Doppler function on the older ultrasound machine. Therefore, the pattern of vascularity in benign and malignant disease cannot be reliably determined from the data. Lesions with high pulsatility and resistive indices are considered to have a higher risk of malignancy; chaotic and disorganized flow was considered a feature of malignancy. Peripheral distribution of vascularity may be seen in both pleomorphic adenomas and malignancy. Warthin’s tumours have hilar distribution with vessels within internal septa. It should be noted, however, that recent studies have found no significant differences in the vessel type or distribution between benign and malignant lesions.

The diagnostic difficulties in determining whether certain lesions are benign or malignant and in differentiating pleomorphic adenomas from Warthin’s tumours are also encountered with computed tomography (CT) and magnetic resonance imaging (MRI). The results obtained from ultrasound examinations can guide the need for further imaging for local and distal staging in patients with malignant disease, those with lymphoma underwent...
CT staging of the neck, chest, abdomen and pelvis; those with non-lymphomatous malignancies underwent distal staging with CT, and in the cases of primary head and neck lesions, the patients also underwent local staging with MRI. Ultrasound also detected additional impalpable parotid disease or lymphadenopathy, confirming that it is an important adjunct to clinical examination.

Potential weaknesses of the present study are that the ultrasound examinations were performed by a single operator and the time over which the study was conducted with the improvements in grey-scale and Doppler during that period, which may have affected the operator's ability to diagnose parotid lesions on the sonographic features. Conversely, the use of a single operator potentially makes the application of a diagnostic algorithm more robust.

In conclusion, the majority of parotid neoplasms are benign and consist predominantly of pleomorphic adenomas and Warthin’s tumours, although distinguishing these lesions on sonographic appearances alone is often not possible and false-negative and false-positive results do occur. However, ultrasound is able to reliably identify a focal lesion; determine whether a lesion is malignant with a high sensitivity and specificity; identify focal lesions that were not clinically palpable, as well as previously unsuspected cervical adenopathy; and guide the need for needle biopsy and further imaging. Ultrasound acts as an important adjunct to clinical examination but, in most patients, should be combined with needle biopsy to maximize diagnostic yield. In some patients, the elderly or in those where biopsy is hazardous, expectant management may be appropriate where clinical and sonographic findings suggest benign disease.

Acknowledgements

The authors thank Professor Andy Grieve for his assistance with the statistical analysis.

References

4.3 Westerland O, Howlett D C

Sonoelastography Techniques in the Evaluation and Diagnosis of Parotid Neoplasms

European Radiology 2012; 22 (9) 66-969
A.Mandy@brighton.ac.uk

Subject: David Howlett PhD by publication

Dear Anne

Re: Westerland O, Howlett D C.
Sonoelastography techniques in the evaluation and diagnosis of parotid neoplasms.

I am writing to confirm that David Howlett made a significant contribution to the above paper. David was involved in the conception and design of this review article, critcally revised the final version for important intellectual content and finally approved the version to be published.

With best wishes.

O. Westerland

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Sonoelastography techniques in the evaluation and diagnosis of parotid neoplasms

Olwen Westerland · David Howlett

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Abstract Ultrasound is the first-line imaging investigation in the evaluation of parotid gland lesions; however, ultrasound alone cannot differentiate between benign and malignant lesions. An imaging technique with this capability would be of great value, as fine needle aspiration cytology (FNAC) is not always accurate and partial/total parotidectomy is associated with facial nerve palsy and Frey’s syndrome. Sonoelastography is a novel imaging technique that has been employed in the research setting in the evaluation of tissues including breast, thyroid, prostate and the salivary glands. More recently it has been used as a diagnostic adjunct in the sonoelographic evaluation of major salivary gland lesions. This review article outlines the current role of sonoelastography in the diagnostic imaging of parotid lesions, with particular reference to the findings of two research papers published in European Radiology. These papers employ slightly different techniques: the first utilises shear wave elastography whilst the second uses real-time sonoelastography. Sonoelastography may have potential as a diagnostic imaging adjunct to conventional ultrasound; however, it seems likely that FNAC/core biopsy will continue to be necessary. Further studies to evaluate the reproducibility of sonoelastographic results across a range of operators and systems are also needed.

Key Points
- **Ultrasound is the initial and often definitive investigation for parotid lesions**
- **Ultrasound-based strain elastography has been attempted but offered little additional information**
- **New shear wave elastographic techniques did not confer much advantage either**
- **However, analysis of elastographic patterns seems to provide advantage over ultrasound alone**

Keywords Ultrasound · Elastography · Shear wave · Parotid · Salivary

Salivary gland tumours account for only 3% of head and neck tumours and 80% of these arise in the parotid gland [1]. They frequently pose a significant diagnostic challenge as there is a wide range of potential differential diagnoses and, while most lesions are benign (approximately 80% of parotid lesions), whether clinical or imaging assessment can reliably differentiate between benign and malignant parotid masses.

A patient presenting with a parotid mass should undergo triple assessment, namely clinical examination followed by imaging (usually ultrasound initially), and if a mass is confirmed will proceed to image-guided needle biopsy to confirm the diagnosis (fine needle aspiration cytology, FNAC, or core biopsy). Magnetic resonance imaging (MRI) or computed tomography (CT) are used to further evaluate large or suspected malignant lesions and to further stage the neck and chest in malignancy. The type of operation undertaken will depend on the type of tumour and also its size and position. Newer surgical techniques such as extracapsular dissection are less invasive than more traditional superficial parotidectomy but an accurate preoperative diagnosis is essential to allow appropriate planning and informed patient consent.

What does the surgeon want from parotid imaging? The technique needs to be highly accurate, sensitive and specific in terms of diagnosis, and also needs to be able to discriminate...
lesions into either the superficial or the deep lobe, and to establish the relationship of the lesion to intraparotid vessels and the facial nerve. An imaging technique that can reliably differentiate benign from malignant disease and also predict benign parotid tumour subgroups (pleomorphic adenoma vs. Warthin’s tumour) would be of great value, and might be able to reduce the need for needle biopsy, which is relatively invasive. Furthermore, FNAC in particular can be associated with high non-diagnostic rates outside of specialist units. Imaging findings alone could then be used confidently to help select the appropriate operative approach and to identify which patients should undergo cervical lymph node dissection.

The ability of an imaging technique to differentiate between pleomorphic adenoma (a benign lesion but with pre-malignant potential) and benign Warthin’s tumour could allow patients to the latter subgroup to avoid surgery. This would be of particular use in the elderly, in poor operative candidates and in those who do not want surgery.

A full discussion of the strengths and weaknesses of various imaging techniques is beyond the scope of this article. Ultrasound is largely accepted as the initial imaging investigation of choice. Imaging techniques alone can achieve diagnostic accuracy rates of approximately 90% (ultrasound) and these approach 100% when combined with needle biopsy [2].

Recent research has evaluated the use of MR peak enhancement curves, diffusion-weighted MR imaging and MR spectroscopy in differentiating between benign and malignant lesions. For example, it has been shown that, in a research setting, dynamic contrast-enhanced MRI can be used to differentiate between malignant salivary gland tumours and pleomorphic adenomas with sensitivity and specificity rates of greater than 90% [3]. While the initial results in MR studies, in differentiating between benign and malignant lesions are promising, these studies were all based on small patient cohorts. Also, both CT and MRI pose additional patient safety risks, cannot be tolerated by all patients and can result in delayed definitive treatment (particularly with MR, as availability is usually limited and immediate imaging may not always be possible, unlike ultrasound which is a readily available imaging technique).

An additional sonoanatomographic technique with the ability to improve upon the diagnostic yield of conventional grey-scale/colour Doppler ultrasound would be of great value.

Sonoechography is a novel imaging technique that can map the elastic properties of soft tissues [4]. A mechanical force (usually manual compression via the ultrasound probe, although vibration can also be used) is applied to the area of interest, following which the degree and distribution of tissue deformation or tissue stiffness is detected and characterized sonoanographically. This is represented visually as an elastogram corresponding to a predefined region of interest, where stiff areas appear dark and soft areas appear bright. The technique is performed using a 5- to 12-MHz linear array transducer and compatible ultrasound machine, with transducer and patient positioning as per conventional B-mode ultrasound [5].

Sonoechography may be performed in real time, where a dual display screen is employed and the elastogram is shown adjacent to its corresponding greyscale sonogram. Real-time imaging provides a qualitative measure of tissue stiffness. Alternatively, image processing can be performed in order to eliminate artefacts, and the resultant elastogram is an average of the processed images, giving a more accurate representation of tissue strain. However, this technique is time-consuming and it is likely that real-time sonoelastography would be better suited to the realities of daily clinical practice [5].

Sonoechosonography is a difficult technique and is vulnerable to intra- and inter-operator discrepancy. Lateral and out-of-plane motion results in image artefact and degrades the elastogram representation. Additionally, the operator must apply a uniform compressive force with each study.

Sonoechosonography has shown promising results in the research setting, for example in the evaluation of breast and prostate malignancy and in the diagnosis of thyroid nodules [6, 7]. While initial results of several studies have been promising, sonoechosonography has not yet found routine usage in wider clinical practice. Reasons for this may include clinician/radiologist awareness of sonoelastography and its potential uses, the need for operator training in what is regarded as a challenging technique and cost implications. There are relatively few published data regarding the use of sonoelastography in parotid gland evaluation. Previously, studies by Blaiia et al. [5] and Dumitru et al. [1] had shown that although parotid malignancies were commonly stiffer than benign lesions, there was significant overlap between elastographic properties of benign and malignant parotid lesions, and the technique overall appeared to have a fairly limited utility in the imaging of the salivary glands.

In the prospective study by Blaiia et al. [5], 65 salivary gland masses (57 parotid, 8 submandibular) were evaluated using real-time qualitative sonoelastography in addition to B-mode ultrasound, before FNAC or core biopsy. Whilst all three primary malignant parotid lesions within the cohort were found to have high sonoelastographic values, the same degree of tissue stiffness was also noted in 16 out of 24 pleomorphic adenomas. They ultimately concluded that this technique would not be useful in differentiating benign from malignant parotid lesions.

Dumitru et al. [1] also used real-time sonoelastography and B-mode ultrasound in the prospective evaluation of salivary gland lesions (38 parotid, 13 submandibular gland), but primarily focused upon identifying a typical sonoelastographic pattern for pleomorphic adenomas. The results of
the sonoelastography component of their study were again disappointing. 31.3% of pleomorphic adenomas were predominantly stiff, as were 53.9% of primary malignancy tumours, 61.3% of which were in the parotid gland (the remainder were submandibular lesions).

Dumitrin et al. also performed a second study [8], in which a cohort of 66 patients with salivary gland tumours (63 parotid, 11 submandibular) was evaluated using real-time sonoelastography and conventional ultrasound. A four-point elastography score was used to grade the lesions. Initially, there was thought to be a statistically significant difference between elastography scores for benign and malignant lesions; however, detailed analysis failed to provide consistent results. For example, the difference in elastography grade for pleomorphic adenomas compared with both Warthin’s tumours and malignant lesions was not statistically significant.

Two recent papers published in European Radiology, looking at variations on the sonoelastography theme in the salivary glands, make further important contributions to this subject. The first utilizes shear wave elastography (SWE) rather than pure strain elastography [9]. In SWE, the applied mechanical force consists of focused pulses of ultrasound waves termed “push pulses” instead of the compressive force of the transducer probe. This induces shear waves which are detected by an ultrasound ultrasound imaging technique. This is thought to be more accurate than strain elastography as it produces quantitative estimates of stiffness and does not rely upon manual compression by the operator.

This technique was used in the prospective assessment of 60 salivary lesions, 49 of which were in the parotid gland and the remainder in the submandibular gland. Grey-scale and colour Doppler imaging were also performed, and results were compared with cytology. Conventional ultrasound examinations were performed by head and neck radiologists, whilst sonoelastography was performed and interpreted by one of three radiologists with over 2 years’ experience in strain elastography and 3 months’ experience in SWE. It should be noted that the authors were blinded to the results of cytology during image interpretation. There were 55 benign lesions (21 pleomorphic adenomas, 18 Warthin’s tumours and 16 others) and 5 malignant lesions (2 mucoepidermoid carcinomas, 1 myoepithelial carcinoma, 1 B cell lymphoma and 1 nodal melanoma). Unfortunately there was considerable overlap of alone wave values between benign and malignant lesions: the median shear modulus of benign lesions was 18.3 kPa (range 0.0–59.4 kPa), compared with a median shear modulus of 15.5 kPa in malignant lesions (range 8.6–132 kPa). However, pleomorphic adenomas were shown to have significantly higher elasticity values compared with Warthin’s tumours (22.5 kPa and 16.9 kPa respectively). Ultimately, the authors concluded that SWE was a suboptimal technique for differentiation of benign and malignant salivary gland lesions.

The second paper used conventional sonoelastography in addition to B-mode ultrasound to try and both differentiate between benign and malignant parotid lesions and establish characteristic elastographic patterns for different types of lesions, with comparison with histology [10]. Fifty-seven patients with parotid tumours underwent B-mode, colour Doppler and elastographic ultrasound. Sonoelastography was performed in real time, using manual transducer compression. All ultrasound and sonoelastographic examinations were performed by two experienced operators, who also interpreted the images. Contrary to the previous study, image interpretation was performed with operator knowledge of lesion histology. The commonest histology type was pleomorphic adenoma (30.4%) followed by Warthin’s tumour (25.4%). Seventeen per cent of lesions were primary parotid malignancies. The remainder of the lesions consisted of other types of benign tumours. Looking at conventional grey-scale ultrasound characteristics, only an indistinct or “blurred margin” could differentiate between benign and malignant lesions with statistical significance. Of the sonoelastically malignant lesions only 3 demonstrated an elasticity pattern the authors termed the “garland sign”, defined as a reticular distribution of stiff tissue within the lesion. However, the Garland sign was only seen in 2 of the remaining 47 benign tumours. This in itself was statistically significant; however, caution was advised as the remaining 5 malignant lesions did not demonstrate this sign, and also gives the small number of malignancies in their cohort.

This study also highlighted several other elastographic appearances seen frequently in specific benign parotid lesions. For example, 19 out of 22 pleomorphic adenomas demonstrated a “dense core” sign (centrum of stiff tissue) and 8 out of 20 Warthin’s tumours a “bull’s-eye” sign (diffuse area in the superficial half of lesion, soft area in the deep half), and these were statistically significant findings. All 3 parotid cysts were described as having a “bull’s-eye” appearance; however, it was not possible to establish the significance of this, because of the small number of parotid cysts in the cohort. Whilst the above results appear promising, the authors themselves have cited several limitations to this study. These included, in addition to the small patient cohort, the fact that sonoelastography using manual transducer compression is an operator-dependent technique, the inter-operator variation in elastographic pattern recognition and the fact that operators were aware of the lesion histology results. Additionally it should be noted that the extent to which these patients may be reproduced using different equipment is not yet known.

In conclusion, sonoelastography is a novel, supplementary adjunct to conventional ultrasound. Initial results looking purely at sonoelastography with or without shear wave techniques in the parotid glands have been disappointing. However, recent work focusing on identifying characteristic
References


4.4 Buckland J R, Manjaly G, Violaris N, Howlett D C

Ultrasound – Guided Cutting Needle Biopsy of the Parotid Gland

Journal of Laryngology and Otology 1999;113: 988-992
Subject: David Howlett PhD by Publication

Dear Anne,

Re: Buckland J R, Manjaly G, Violaris N, Howlett D C


I am writing to confirm that David Howlett made a significant contribution to the above paper. David was responsible for study conception and design, together with data acquisition. He was also involved with data analysis and interpretation, critically revising the paper and approving the final published version.

With best wishes,

Mr George Manjaly. MPhil, FRCS (1) FRCS (ORL) Eng
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Ultrasonsound-guided cutting-needle biopsy of the parotid gland


Abstract
We describe the technique of ultrasound-guided 18 gauge (1.2 mm) needle biopsy in 16 patients with parotid gland lesions. This provides material suitable for histological analysis and can be performed quickly and safely under local anaesthesia. Thirteen of the patients had non-diagnostic fine-needle aspiration cytology (FNAC) with a 21 gauge (0.8 mm) needle prior to biopsy. Initial ultrasound was found to be superior to clinical examination in 31 per cent of cases. The ultrasound-guided technique provided a diagnostic specimen in 100 per cent of patients and was helpful where FNAC had been inconclusive. There was a diagnostic accuracy of 100 per cent in the patients who underwent subsequent surgery. This method should be considered when FNAC is non-diagnostic and surgical treatment is being considered. It is particularly useful in patients with diffuse enlargement of the gland and does provide a core of material for accurate assessment of tissue architecture. In this series, nine patients avoided unnecessary surgery.

Key words: Parotid gland; ultrasonography; biopsy; Neoplasms metastatic

Introduction
Parotid gland lesions are a histologically diverse group. Tumours of this region comprise three per cent of all head and neck tumours and 0.6 per cent of all tumours of the human body (Hugo et al., 1975). If a surgeon can obtain an accurate diagnostic biopsy then he is able to make an informed decision with regards to surgical intervention.

A large number of these lesions, particularly those in the superficial part of the gland, are readily palpable and easily accessed.

The traditional open biopsy is no longer justified because of the risk of tumour spillage (McQuirt and McCabe, 1978) and damage to the facial nerve. FNAC is an established technique but usually provides material for cytological analysis only.

An alternative is to take a core of tissue using a small cutting-needle. Needle placement is more precise when combined with ultrasound. We describe the use of the ultrasound-guided cutting-needle biopsy in the work up of a series of patients with parotid lesions.

Materials and methods
Over a one-year period (February 1998-February 1999), 16 patients were referred for biopsy. Referrals came from a variety of specialties – one general medical in-patient, one maxillo-facial out-patient and 14 ear, nose and throat out-patients. Patients ranged in age from 17 years to 84 years (mean age 55 years). There were four females (25 per cent) and 12 males (75 per cent). The biopsy service was initially developed for patients who had had a non-diagnostic FNAC.

All the patients had clinically palpable lesions of the gland – either a discrete unilateral lesion (12 patients) or more diffuse bilateral swelling (four patients). Patients gave written consent for the procedure, having been warned of the possibility of haemorrhage and facial nerve damage. The same protocol was used throughout.

A single operator (D.C.H.) performed both the ultrasonography and biopsy. Initial ultrasound scanning was done using an ATL Ultrasound-9 machine and a 5-10 MHz high frequency linear array transducer. Biopsies were taken using a spring-loaded 18 gauge (1.2 mm) biopsy gun (BIOPTY, BARSD) with a 20 mm throw.

Having identified the position of the lesion, the overlying skin and subcutaneous tissues were infiltrated with one per cent lignocaine. A small skin incision was made to facilitate insertion of the needle. The scanning probe was positioned over the lesion and using the dominant hand the biopsy needle was guided into the mass and discharged (Figure 1).

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Results

Initial fine-needle aspiration cytology

Thirteen of the 16 patients (numbers 1 to 13) had 'blind' FNAC performed by the referring surgeon prior to referral for ultrasound guided biopsy. The aspirates were taken using a 21 gauge (0.8 mm) needle. None of the aspirates provided definitive cytology. In one case (patient 1), a provisional diagnosis of squamous carcinoma was made. All the remaining samples were non-diagnostic. The most common problem was blood only in the aspirate. The one positive cytology did not correlate with the final histology (see Table 1). Patients 14 to 16 were referred directly for biopsy without FNAC.

Initial ultrasound scanning

Ultrasound was found to be an effective way of identifying the size and location of the lesion. In the 12 patients with discrete, unilateral swellings these ranged in size from 6 mm to 45 mm (maximum diameter). All were noted to arise from the superficial part of the gland and none were extra-parotid. Additional lesions that were clinically palpable were detected by US in three patients. In the four patients with clinically diffuse, bilateral disease, US identified a discrete lesion in two patients.

On US the lesions were generally heterogeneous, hypoechogenic solid except in three cases where cystic components were also seen. Ultrasound allowed accurate placement of the needle for biopsy in all cases. The average scan plus biopsy time was 15 minutes.

Table 1: A comparison of histological results in the patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Blind FNAC</th>
<th>Ultrasound-guided core biopsy</th>
<th>Final outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Squamous carcinoma within a lymph node (provisional)</td>
<td>High grade muco-epidermoid carcinoma</td>
<td>Micro-epidermoid carcinoma at parotidectomy</td>
</tr>
<tr>
<td>2</td>
<td>Non-diagnostic</td>
<td>Fatty infiltration</td>
<td>Under observation</td>
</tr>
<tr>
<td>3</td>
<td>Non-diagnostic</td>
<td>Warthin’s tumour</td>
<td>Thought to be alcohol-related</td>
</tr>
<tr>
<td>4</td>
<td>Non-diagnostic</td>
<td>Granulomatous inflammation</td>
<td>Elderly, under observation</td>
</tr>
<tr>
<td>5</td>
<td>Non-diagnostic</td>
<td>Adenocarcinoma</td>
<td>Possible sarcomatous</td>
</tr>
<tr>
<td>6</td>
<td>Non-diagnostic</td>
<td>Pleomorphic adenoma</td>
<td>On treatment</td>
</tr>
<tr>
<td>7</td>
<td>Non-diagnostic</td>
<td>Fatty infiltration</td>
<td>Micro-epidermoid carcinoma at parotidectomy</td>
</tr>
<tr>
<td>8</td>
<td>Non-diagnostic</td>
<td>Benign cyst</td>
<td>Pleomorphic adenoma</td>
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<td>Granulomatous inflammation</td>
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<tr>
<td>10</td>
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<td>Normal parotid tissue</td>
<td>Pleomorphic adenoma</td>
</tr>
<tr>
<td>11</td>
<td>Non-diagnostic</td>
<td>Granulomatous lymphadenitis</td>
<td>On treatment</td>
</tr>
<tr>
<td>12</td>
<td>Non-diagnostic</td>
<td>Adenoid cyst carcinoma</td>
<td>Adenoid cyst carcinoma at parotidectomy</td>
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<tr>
<td>13</td>
<td>Non-diagnostic</td>
<td>Pleomorphic adenoma</td>
<td>Pleomorphic adenoma</td>
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<tr>
<td>14</td>
<td>Not performed</td>
<td>Warthin’s tumour</td>
<td>Warthin’s tumour at parotidectomy</td>
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<tr>
<td>15</td>
<td>Not performed</td>
<td>Fatty infiltration</td>
<td>Warthin’s tumour at parotidectomy</td>
</tr>
<tr>
<td>16</td>
<td>Not performed</td>
<td>Warthin’s tumour</td>
<td>Warthin’s tumour at parotidectomy</td>
</tr>
</tbody>
</table>
Histology

A summary of the cytological and histological findings are presented in Table 1. In 100 per cent of cases tissue was obtained for histology. No samples were 'inadequate' (i.e. no tissue or insufficient for analysis). Thirteen benign and three malignant diagnoses were made. Of the 15 patients who had non-diagnostic FNAC all had a diagnosis made on core biopsy. Of the patients who had bilateral disease, all had benign histology on core biopsy.

We were able to compare the core biopsy result to a final operative specimen result in seven patients. The core biopsy was 100 per cent accurate in the differentiation of benign from malignant disease. There was one case (patient 5) in which core biopsy did not correlate precisely with the operative histology. Although the biopsy diagnosed a carcinoma (adenocarcinoma) the final histology was a mucoepidermoid carcinoma. Nine patients have avoided surgery as a direct result of the biopsy. Three particularly interesting patients were diagnosed with granulomatous inflammation. Although no firm diagnosis has been established two are thought to be secondary to sarcoid and one is undergoing treatment with anti-tuberculous chemotherapy. Patient 3, an elderly and medically unfit man has been closely followed up in outpatient. Patient 10 had a diffuse swelling of the parotid following radiotherapy for a tonsillar carcinoma.

Complications

There were no immediate complications. One patient, at the time of superficial parotidectomy, was found to have a resolving haematoma and this made the procedure technically more difficult.

We are not aware of any local seeding.

Discussion

Ultrasound of the parotid

Diagnostic ultrasound is a fast, non-invasive and multiphasic imaging modality that helps in the assessment of palpable and impalpable parotid lesions. During scanning, the margins of the gland can appear rather indistinct but parotid tissue is easily distinguishable from the adjacent maseter and mandible. The deep lobe is obscured by the mastoid process and mandible since sound is reflected by bone. For this reason, ultrasonography cannot reliably demonstrate deep lobe masses (Nettle and Orell, 1989). Superficial lesions can be accurately localized (as either intra or extraglandular) and sized (Rothberg et al., 1984; Cvetinovic et al., 1991). The ability of ultrasonography to differentiate between the various pathological processes is less clear. It readily demonstrates diffuse enlargement and can aid the morphological assessment of focal disease. Solid and cystic lesions can be differentiated. Ultrasonography may also be useful in the assessment of reactive parotid adenopathy. Reactive nodes tend to be multiple and ovoid with a well-defined, central, echogenic fatty hilum. It may detect otherwise impalpable lesions and can be helpful where there is diffuse enlargement of the gland as in our study. It is unable to determine the location of the facial nerve (Rothberg et al., 1984) but damage to this during ultrasound-guided biopsy has not been reported and we have encountered no problems (McIvor et al., 1994; Bearcroft et al., 1995; Elvin et al., 1997). It is possible to demonstrate lesions as small as 0.5 mm (Rothberg et al., 1984) or less, with newer high frequency transducers. We found ultrasound a useful initial screening tool prior to biopsy. Magnetic resonance imaging is complementary to ultrasound in the assessment of parotid lesions but has the advantage of being able to visualize the deep lobe (Byrne et al., 1989).

Ultrasound-guided biopsy

The value of ultrasound-guided biopsy is now well established due to its ease of use and real-time capability (Lindgren, 1980). It has several advantages over blind biopsy. The lesions can be approached safely from a variety of angles. Smaller and impalpable lesions can be biopsied and the needle can be confidently guided into the lesion (Elvin et al., 1997). As a consequence, ultrasonography improves the accuracy of biopsy (Matilann and Silver, 1990). Ultrasonography can be particularly useful when trying to localize the needle for aspiration of cystic lesions. It has been suggested by some authors that it does not improve the adequacy of sampling for palpable lesions (McIvor et al., 1994).

In our study, it was apparent that discrete lesions appeared generally hypoechoic and heterogeneous with ultrasonography. When performing the biopsies we attempted to take a representative sample from the centre of the lesion rather than the periphery. Previous work involving cervical lymph node has shown that if ultrasonography demonstrates that a lesion has a central core, then biopsies taken from the centre are more likely to be adequate than those taken from the periphery (McIvor et al., 1994). In our study, with the knowledge that the biopsy needle had a 20 mm throw, it was possible to ensure that the needle was placed such that biopsy traversed, but did not exit the mass. Ultrasonography may be used post-biopsy to monitor for complications such as haematoma (Bearcroft et al., 1995) and colour doppler can give information on potential vascular abnormalities and demonstrate vessels entering the hilum of a reactive lymph node.

Fine-needle versus core-biopsy

Our study did not directly compare ultrasound FNAC to ultrasound core-biopsy. The technique of fine-needle aspiration biopsy is well described in the literature (Fralbe, 1983). The standard procedure is to use a fine needle of 21 gauge (standard wire gauge: 0.8 mm) or less. Core-needle biopsy utilizes larger needles of 18 gauge (1.2 mm) or greater.

There is now an established role for FNAC in salivary gland lesions (Simonis et al., 1980; Roland et al., 1993). Several limitations are apparent. Firstly, the technique requires an expert cytologist and the
aspirate is probably best taken in a special clinic (Roland et al., 1993). If the aspirations are performed by a surgeon and then subsequently reported by a cytopathologist (as in our study), there may be a number of inadquate specimens (with insufficient material to make a diagnosis). These may be as high as 14–15 per cent even with ultrasound guidance (Roland et al., 1993; McVor et al., 1994). Thirteen of our cases had non-diagnostic blind FNAC. Given the large number of aspirations performed each year this may not represent a high proportion but may relate to our technique and lack of an immediate reporting facility. Diagnostic accuracy is in the range of 85–90 per cent (Shemans et al., 1981; O’Dwyer et al., 1989). Secondly, a FNAC may miss a critical area within the mass and give a false negative result. Sensitivity varies widely from 64 per cent (Eneroth et al., 1987) to 100 per cent (Webb, 1973). False positive results are rarely reported but may result from atypia in benign mixed tumour (O’Dwyer et al., 1986).

In other parts of the body (e.g. breast) Tru-cut biopsy has been shown to be superior to FNAC in the diagnosis of certain cancers (Sadler et al., 1994). Ultrasound-guided core biopsy provides adequate specimens in up to 99 per cent of cases and histological examination of fine-needle core biopsy can provide more accurate information about cell type and tissue characteristics than aspiration cytology (Jennings et al., 1989). This can be particularly important where tissue architecture is needed e.g. lymphoma (Beacroft et al., 1993). In one study, the cutting needle was found to be advantageous because it was rapid and did not require multiple passes therefore reducing patient discomfort (Jennings et al., 1989).

It is difficult to make direct comparisons between FNAC and core biopsy because both are clearly operator dependent. Some studies use ultrasound guidance whilst others do not. Some studies bias the results by removing the inadequate samples from their analysis of data.

In our series, ultrasound-guided core biopsy with the 1.2 mm needle provided a diagnostic specimen in 100 per cent of patients and was superior to blind FNAC in 13 patients. One distinct advantage of this was that we were able to plan treatment appropriately and to identify unusual pathology. Nine patients avoided surgery from the information given by the biopsy. Three patients (numbers 4, 9, and 11) had granulomatous inflammation. Three patients (numbers 2, 7 and 15), all of whom had bilateral parotid swelling, had lymphyadenolysis. One benign cyst (patient 8), one Warthin’s tumour (patient 3) and one radiation-related parotid swelling (patient 10) have been monitored in out-patients.

Seeding

One main concern over any biopsy is the possibility of seeding. Jacksonian biopsy is associated with an unacceptably high risk of tumour seeding (McGurk and McCabe, 1973). Reports of seeding along a needle tract seem to relate mainly to needle size. It is rare with needles of less than 1.0 mm.

Presumably this is because stromal fragments, necessary for survival of cancer cells, are removed (Naikkhonya and Zahour, 1991). Other factors may include the number of passes (Rashleigh-Beicher et al., 1986). Even with fine needles of 22 gauge (0.8 mm) cutaneous seeding is still a possibility (Glaser et al., 1989; Rashleigh-Beicher et al., 1991). However, whilst there are no reported cases of seeding following FNAC of salivary gland tumours there have been sporadic cases of seeding using a 14 gauge Tru-cut needle or Vim-Silverman needle (Fralbe, 1976; Yamaguchi et al., 1979). We are not aware of any cases of seeding using an 18 gauge needle and previous papers using a similar technique to biopsy head and neck lesions have not reported this complication (Beacroft et al., 1995; Elvin et al., 1997).

It has been suggested that the number of dry passes (when no material is obtained) is lower with a larger needle (23 gauge) but that diagnostic quality of the aspirate may be superior with a smaller needle (22 gauge). However, this study looked at the thyroid gland and this may not necessarily apply to the parotid gland (Hasbridge et al., 1995).

There are no reports of facial nerve weakness following core biopsy. One case of subclinical haemotoma has been described elsewhere (Beacroft et al., 1995).

Conclusions

We have found the technique of initial ultrasound-guided core biopsy to be useful in the work up of a series of patients with parotid masses. Ultrasound-guided core biopsy is easier than clinical palpation in the assessment of the gland. Ultrasound-guided core biopsy has a lower non-diagnostic rate than blind FNAC and tissue obtained correlates well with final histology.

One of the considerations in parotid surgery is that pre-operative diagnosis may influence the decision to undertake conservative or radical surgery and unnecessary surgery may be avoided. A recent survey of head and neck surgeons found that there is a lack of consensus regarding the role of FNAC in the diagnosis of parotid tumours (McGurk and Husaana, 1997) and it is well known that the majority of salivary gland swellings are excised (Illes and Brisan, 1986).

The role of ultrasound-guided core biopsy may perhaps be best utilized when FNAC is unhelpful or in patients with diffuse parotid gland disease where a systemic pathology is suspected and where surgery may then be avoided. It may also be considered in institutions without a dedicated FNAC service.

Our data would suggest that pre-operative ultrasound-guided core biopsy may reduce the number of patients requiring surgery for parotid lesions.

Acknowledgement

The authors would like to thank Mike Sibson for his assistance.
4.5 Kesse K W, Manjaly G, Violaris N, Howlett D C

Ultrasound Guided Biopsy in the Evaluation of Focal Lesions and Diffuse Swelling of the Parotid Gland

A Mandy@brighton.ac.uk

Subject: David Howlett -PhD by Publication

Dear Anne

Re:  Kesse W, Manjaly G, Violaris N, Howlett D C

Ultrasound Guided Biopsy in the evaluation of focal lesions and diffuse swelling of the parotid glands.

I am writing to confirm that David Howlett made a significant contribution to the above paper. David was responsible for study conception and design and data acquisition. He assisted with data analysis and interpretation together with critical revision of the final version which he also approved.

With best Wishes

Mr George Manjaly MPhil FRCS.
Consultant ENT Surgeon
Eastbourne District General Hospital
Eastbourne
East Sussex
BN21 2UD
Ultrasound-guided biopsy in the evaluation of focal lesions and diffuse swelling of the parotid gland

K. W. Kesse, G. Mampali, N. Vichurs, D. C. Howlett

*Department of Otolaryngology, †Consultant Radiologist, Department of Radiology, Eastbourne District
General Hospital, Eastbourne, UK

SUMMARY: We describe the technique of ultrasound-guided core biopsy with a spring-loaded device in 54 patients who presented with palpable lesion of the parotid gland. Biopsy provided a sample suitable for histological analysis in all patients and was done quickly and safely under local anaesthesia. Initial diagnostic ultrasound confirmed the presence of focal palpable lesions and identified additional impalpable lesions in seven patients. Core biopsy was 100% accurate in differentiating benign from malignant disease. The diagnosis was accurate in 27 of the 28 patients who were subsequently operated on. Twenty-six patients avoided an unnecessary operation. The technique is also useful in patients with diffuse enlargement of the parotid gland and provides a core of tissue for accurate assessment of tissue architecture.

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INTRODUCTION

Various pathological conditions may present with palpable swelling in the parotid region. These swellings may be neoplastic or benign, and intra-glandular or extra-glandular. Parotid gland neoplasms are uncommon and the WHO classification recognised 12 benign and 22 malignant primary epithelial neoplasms together with various tumour-like lesions, lymphoproliferative disorders, and metastatic tumours. The different types of salivary gland tumour are distinct in their clinical behaviour and response to treatment. Histological diagnosis therefore weighs heavily on therapeutic decision making and prognosis.

The symptomatic evaluation of benign and malignant discrete parotid swelling is usually similar. Occasional findings such as unusual firmness or V1 nerve involvement may strongly suggest malignancy, but it is rarely possible to predict the histological type with any degree of certainty on clinical examination alone. For histological diagnosis, samples can be obtained by open biopsy or needle aspiration. Open biopsy of tumours of the parotid gland is no longer justified because of the risk of spillage of tumour cells, VII nerve damage, facial scar, and tritidal development. Fine needle aspiration cytology (FNAC) of the parotid gland, however, is an established technique. It may be blind or guided by ultrasound to allow accurate placement of the needle, but the material obtained by FNAC is usually for cytological analysis only. An alternative is to take a core of tissue with a small cutting-needle under ultrasound guidance. In this study we describe the role of ultrasound-guided core-biopsy with a spring-loaded device in the management of palpable parotid lesions.

PATIENTS AND METHODS

From February 1998 to July 2001, 54 patients with palpable parotid swellings were entered into this prospective study. The biopsy service was initially developed for patients who had had a non-diagnostic blind FNAC. The age range was 18–92 years (mean 55 years) with equal distribution of men and women. All patients had clinically palpable swelling of the parotid gland, which was either unilateral (n = 48) or bilateral (n = 6). Patients gave written consent for the procedure having been warned of the possibilities of haemorrhage and damage to the facial nerve. A single operator (DCH) performed both ultrasound and biopsy. Initial ultrasound was done using a 5–10 MHz high frequency linear array transducer. This was followed by guided biopsy under local anaesthesia. In the first 16 patients a Biopsy Gun (Bard) with a 22 mm fixed throw and fitted with an 18 G needle was used. Biopsy in the remainder of the patients was with a Magnum Gun (Bard) with a variable throw (15 or 22 mm) fitted with a 20 G needle. The position of the lesion was identified, and the overlying skin and subcutaneous tissue were anaesthesised with 1% lignocaine. The scanning probe was positioned over the lesion and the dominant
hand was used to guide the biopsy needle into such a position that the needle would traverse but not exit the mass. This ensured a sample was obtained to include the periphery and core of the lesion. We made a mean of 2 passes of the needle (patient range 1–3). The specimens were immediately fixed in formaldehyde. Patients were observed for 1 h after the procedure. The scan and biopsy usually took about 15 min.

### RESULTS

The first 16 patients in this series had non-diagnostic un-guided FNAC with a 21 G (0.9 mm) needle by the referring clinician before ultrasound-guided core biopsy. The most common problem was aspirate that contained only blood. Forty-eight patients had clinically discrete palpable uni-lateral prostatic lesions which on ultrasound examination

<table>
<thead>
<tr>
<th>Case number</th>
<th>Core biopsy diagnosis</th>
<th>Postoperative diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pleomorphic adenoma</td>
<td>Pleomorphic adenoma</td>
</tr>
<tr>
<td>2</td>
<td>Warthin’s tumour</td>
<td>Pleomorphic adenoma</td>
</tr>
<tr>
<td>3</td>
<td>Normal parenchyma</td>
<td>Normal parenchyma</td>
</tr>
<tr>
<td>4</td>
<td>Saccular</td>
<td>Saccular</td>
</tr>
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<td>5</td>
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</tr>
<tr>
<td>6</td>
<td>Macropapillary tumour</td>
<td>Macropapillary tumour</td>
</tr>
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</tr>
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<td>8</td>
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</tr>
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<td>Macropapillary tumour</td>
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<tr>
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<td>Fatty infiltration</td>
<td>Fatty infiltration</td>
</tr>
<tr>
<td>11</td>
<td>Teleruption</td>
<td>Teleruption</td>
</tr>
<tr>
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</tr>
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were compartmentalised to the superficial lobe of the parotid; no lesion was outside the gland. The maximum diameters of lesions ranged from 6 to 45 mm. Additional intraparotid lesions that were clinically impalpable were detected by ultrasound in seven patients. Six further patients had clinically diffuse, bilateral parotid swelling and focal abnormalities were not identified sonographically.

**Histopathological correlation**

A summary of the core biopsy and postoperative histological findings is presented in Table 1.

**Complications**

There were no immediate complications that required treatment although one patient at the time of superficial parotidectomy had a resolving subclinical haematocele. No local seeping has been reported since the series was started three and a half years ago and follow-up of patients is continuing.

**DISCUSSION**

High-resolution ultrasound is a safe, multipurpose, and readily available imaging technique used for the assessment of parotid diseases and is able to characterise parotid lesions effectively. It can confirm the presence of a lesion, defines its characteristics better than palpation, and it indicates whether the lesion is within the parotid gland or outside. The normal parotid gland is of homogeneous echopattern and intraparotid ducts and normal intraparotid nodes can be seen. The facial nerve cannot be shown reliably with ultrasound but its location can be inferred, as it lies superficial to the main intraparotid vessels, which are well seen. Lesions may therefore be compartmentalised to the superficial or deep lobe of the gland. During scanning, the margins of the gland can look rather indistinct but parotid tissue is easily distinguishable from the adjacent masseter and mandible. The deep lobe is not well seen with ultrasound, as it is obscured by the mastoid process and mandible and so deep lobe masses are more reliably shown sonographically. Ultrasound is accurate in the initial characterisation of parotid lesions. Solid and cystic lesions are reliably differentiated. Diffuse enlargement of the parotid gland or focal disease is readily shown by ultrasound. Sonographically, benign lesions usually look well-defined, homogeneous, and hypoechoic, while malignant lesions tend to be ill-defined, and hypoechoic with heterogeneous internal architecture, and enlarged cervical lymph nodes may be visible. Reactive intraparotid lymph nodes may also be readily assessed. They tend to be mottled and well-defined with a prominent central echogenic foci.

Ultrasound can be used to guide the needle for further imaging (either computed tomography or magnetic resonance imaging) for large lesions with possible deep lobe extension or for possible malignancy.

To ensure a diagnostic specimen, the needle must pass through the lesion. Central sampling of a solid lesion is more reliable than peripheral sampling. Most palpable parotid lesions, are aspirated by stabilising the lesion with the fingers of one hand while aspirating with the other. Smaller palpable lesions are more difficult to needle and surrounding tissue may be aspirated instead. Aspiration or biopsy under ultrasound guidance circumvents this problem by ensuring that the lesion itself is sampled. This technique offers the ability to sample non-palpable disease, gives access to different regions of a lesion, and approaches the lesion from different angles. The use of a spring-loaded device such as the Biopsy or Magnum gun to dislodge the needle also offers the advantage of precise and co-ordinated cutting action. This combined with ultrasound ensures that the needle is placed so that biopsy traverses, but does not exit the lesion. The variable through facility is useful here for smaller lesions. In this series ultrasound biopsy with 18 or 20 G needle provided a diagnostic specimen in all patients and unusual conditions such as sarcoidosis, Sjögren's syndrome and tuberculosis were diagnosed. Ultrasound also helps to distinguish a mass in the tail of the parotid from other local structures such as lymph nodes and branchial cysts when clinical evaluation is equivocal. In older and incontinent patients confirmation of a non-neoplastic or benign neoplasm will avoid the need for operation.

Preoperative diagnosis of the type of tumour is of value in the management of patients with parotid gland tumours. For most benign lesions compartmentalised with ultrasound to the superficial lobe, superficial parotidectomy is curative. However, partial parotidectomy is considered inadequate in the management of adenoid cystic carcinoma and high-grade malignant tumours. Knowledge of the type of tumour in patients who are considered to be poor surgical or anaesthetic risks is useful in clarifying the need for intervention. This also allows for better planning of the extent of resection as well as allowing for informed consent about the possible risk of permanent damage to the facial nerve.

Salivary gland tumours are relatively rare and few cytopathologists ever obtain the experience needed to diagnose them with confidence and accuracy. Some tumours are characterised by a combination of morphological patterns. In these, limited sampling does not provide a complete representation of the overall morphological picture. Unsatisfactory aspiration is more likely with small lesions, those of low cellularity, and uncommon histology. FNAC has advantages that include minimal tissue damage, no need for anaesthesia, and immediate assessment of adequacy of the sample, and sampling can be repeated.
to obtain a further specimen for culture. FNAC is generally well-tolerated by patients with few complications but it may not provide the full histological diagnosis. Grading and typing of tumour are not possible and, more importantly, it is incapable of distinguishing in situ from invasive malignancy. These conditions may be missed by FNAC, so it has many pitfalls for false positive and false negative diagnoses. The diagnostic accuracy of FNAC of the salivary gland is directly related to the experience of the cytopathologist. It is fairly accurate in broadly distinguishing benign and malignant tumour but accuracy breaks down with more specific tumour classification, with malignant tumours often being misclassified.

Many pathologists prefer to obtain and prepare specimens themselves, which has lead to the development of cytology clinics. With appropriate experience in cytological diagnosis FNAC can distinguish benign from malignant disease in over 95% of patients. However, this degree of cytological specialisation is not routinely available in every hospital, and core biopsy is a viable option, as the technique obtains a core of tissue for analysis. In hospitals that do not specialise in the treatment of parotid neoplasms core biopsy can be used in the diagnosis of malignant lesions to allow referral to an appropriate centre.

The histological results of core biopsy in this series correlated well with the final histological diagnosis in all patients who were operated on except one. In this patient the histological picture of the core biopsy was squamous cell carcinoma while a diagnosis of high-grade mucoepidermoid carcinoma was made in the final specimen. It is well recognised that the diagnosis of primary squamous cell carcinoma of the salivary gland is difficult to establish with unwavering certainty and that high-grade mucoepidermoid carcinoma may be misdiagnosed as squamous cell carcinoma from a biopsy or FNAC specimen. This distinction is problematic for high-grade mucoepidermoid carcinoma with a predilection for anaplastic epithelial cells, where a conspicuous epithelial component may entirely overshadow a minor component of reactive, epithelial cells causing considerable morphological overlap with squamous cell carcinoma. In this instance, the diagnosis of mucoepidermoid carcinoma relies on histochemical demonstration of mucin with tumour cells14 or examination of the specimen ultrasonographically.15 These facilities may not be always available.

Complications

The main objection to biopsy of the parotid gland are the danger of injuring the facial nerve and seeding neoplastic cells. The facial nerve is not reliably seen on ultrasound but its location can be inferred, as it lies superficial to the main intraparotid vessels, which are well seen. Under ultrasound guidance therefore, injury to the facial nerve can be avoided. Intraoral biopsy is associated with a high risk of tumour seeding, particularly of pleomorphic adenomas and carcinomas. Extensive clinical and experimental studies have been done to prove the safety of needle aspiration biopsy,16,17 and there are a number of reports of seeding along the needle tract after aspiration or core biopsy.18,19 These indicate that spreading or seeding of tumour cells after needle aspiration or biopsy is mainly related to the size of the needle.20 The available evidence suggests that this complication tends to occur with large bore needles,21,22 and is rare when 20G or 22G needle (0.6-0.9 mm) are used.23 This is probably because larger bore needles allow aspiration of sizable smaloo fragments, which may play a crucial part in the survival of malignant cells. The risk of seeding also varies according to the anatomical sites, with figures of up to 12% after FNAC of throracic mass,24 and only 0.2% for abdominal tumours.25 Although it is taught that pleomorphic adenoma has a high risk of seeding after core biopsy, we know of only two case reports that describe seeding after biopsy of parotid lesions, and these did not involve fine bore needles.26,27 It should be noted that the local recurrence rate after superficial parotidectomy for pleomorphic adenoma is 2-5%.28,29 This risk is thought to relate to the presence of microscopic pseudopodia that extend outside the capsule rather than capillary breach during the operation.29,30 Smith et al.31 in a series of 100 patients with neck lumps, including 13 parotid lesions, reported no complications after core biopsy using an 18G needle. In our series we used a mix of 18 and 20G needles, which are marginally larger than the 21G needle normally used for FNAC. Other authors who also use cutting needle biopsy in the investigation of head and neck lumps have suggested the inclusion of the needle tract in the subsequent resection.32

REFERENCES


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4.6  Howlett D C

Diagnosing a Parotid Lump: Fine Needle Aspiration Cytology or Core Biopsy?

REVIEW ARTICLE

Diagnosing a parotid lump: fine needle aspiration cytology or core biopsy?

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ABSTRACT. Fine needle aspiration cytology (FNAC) has been widely adopted for the cytological diagnosis of parotid lumps. FNAC does have drawbacks, even under optimum conditions and may be associated with poor levels of diagnostic accuracy, particularly outside of the specialized clinic environment. Ultrasound-guided core biopsy (USCB) is a relatively recently described technique in the parotid gland which has been well validated and has demonstrated a high degree of diagnostic accuracy in several studies. This article discusses the merits and pitfalls of FNAC, together with the technique of USCB and also highlights the potential advantages benefit provided by USCB in parotid diagnosis.

A broad spectrum of pathologies that present with parotid swelling and extraglandular masses can also mimic parotid lesions clinically. It is frequently difficult to distinguish between nonepithelial and non-neoplastic causes for a parotid mass and also to reliably differentiate between benign and malignant neoplasms. If an accurate pre-operative diagnosis can be achieved using a combination of imaging and cytology or histology, then many non-neoplastic lesions will not require excision. Surgery may also be avoided for certain parotid neoplasms in the elderly or unfit, e.g. Warthin's tumour. To ensure that surgery is indicated and to allow appropriate planning and patient consent an accurate pre-operative diagnosis is essential. Following initial demonstration and characterization of a parotid lesion with imaging, usually ultrasound or MRI, needle biopsy is used to confirm its nature if required. Following the demise of open biopsy due to high rates of tumour seeding [1] fine-needle aspiration cytology (FNAC) has become an established technique. FNAC is most commonly performed blindly in the outpatient clinic and has a number of advantages – it is quick, safe and accurate in the hands of a skilled practitioner and high levels of diagnostic accuracy have been quoted [2, 3]. This process may occur within a specialized clinic and diagnostic accuracy can be improved using ultrasound-guidance and an on-site cytologist [4]. Clinics may also be cytologist-led, although this may necessitate multiple aspirations and there is currently a severe shortage of cytology staff available with the necessary expertise, making it difficult to offer this facility outside larger centres.

In the absence of ultrasound-guidance, or an on-site cytologist the diagnostic accuracy of FNAC often falls-off dramatically. A recent study reported a sensitivity of only 38% in distinguishing benign from malignant disease using blind FNAC [5]. There are also well-recognized pitfalls of FNAC even in experienced hands – particular difficulties may occur in the cytological diagnosis of pleomorphic adenoma [7, 8], Warthin's tumour [9] and lymphoma [10]. Indeed the diagnosis of lymphoma with FNAC is not generally considered definitive, with FNAC often acting solely as a guide for the need for surgical biopsy if lymphoid proliferation is present cytologically [11]. There are specialized ancillary cytological techniques, e.g. flow cytometry and in situ hybridization, which are used to improve the diagnosis of lymphoid proliferation but these are not widely available outside larger centres. The cytological diagnosis of parotid involvement by systemic disease, e.g. sarcoidosis and Sjögren's syndrome may be difficult and is not always possible to accurately grade or type malignant tumours or lymphomas or to distinguish the site from invasive disease with FNAC. FNAC has a low predictive value for benign non-neoplastic lesions [3] and similarly there is a low negative predictive value if a negative FNAC result is obtained [4]. As a consequence of the diagnostic difficulties that may arise with FNAC there is a high incidence of surgical biopsy with subsequent delays in referral to the appropriate clinical team.

Performing ultrasound-guided core biopsy (USCB) using a spring-loaded biopsy device does provide a recently described alternative to parotid FNAC. Core biopsy possesses an inherent advantage over FNAC in that it provides a sample of tissue for immunohistochemical analysis. This allows typing and grading of carcinomas and lymphomas and also improved differentiation of reactive nodal hyperplasia from lymphoma. A core of tissue can also be used to evaluate parotid involvement by systemic disease. An on-site cytologist is not required and USCB can be combined with an initial diagnostic ultrasound, allowing lesion characterization and compartmentalization into superficial or deep lobe.
In two series of patients with parotid masses USCR has shown promising results with diagnostic samples obtained in all patients and reported accuracies of 100% [12] and 97% [13] when comparing core biopsy with final surgical histology. There were no reported complications of USCR and 26 out of 54 [12] and 22 out of 55 [13] patients avoided surgery as a result of core biopsy.

USCR utilises a small bore needle (18 G or 20 G) which is introduced through a small skin incision following informed written consent and infiltration with 1% lignocaine local anaesthesia. Using a high-resolution linear-array transducer for guidance, the needle-tip is positioned just adjacent to the lesion, such that following discharge the needle traverses, but does not exit deep to the lesion (Figures 1 and 2). The use of ultrasound is important as it allows avoidance of adjacent structures during biopsy and also ensures that both the periphery and core of the lesion are sampled, with bypassing of necrotic areas, increasing diagnostic yield [12]. Some biopsy devices can allow the needle throw to be varied (Kogoumba gun; Bard, Covington, GA – 15–22 mm variable throw), which is useful for smaller or deeper lesions in proximity to the parotid vessels. There are important potential complications of needle biopsy including haemorrhage and facial nerve injury and also tumour seeding in the needle tract. The identification of the intraparotid vessels on ultrasound should allow the main parotid vessels and thereby the adjacent facial nerve to be avoided during biopsy. There are too reports of tumour seeding post needle biopsy [14, 15] although these occurred with large bore needles and this phenomenon is not described using smaller needle sizes.

Some surgeons may choose to excise the biopsy tract at the time of operation. USCR is a little more invasive than FNAC in that it requires local anaesthesia and a skin incision. USCR also does not lend itself to the ‘one-stop’ clinic setting due to longer requirements for histological reporting than a cytology aspiration.

In conclusion USCR represents a recently described technique for diagnosing a parotid mass which has potential benefits over FNAC. These advantages may be particularly relevant in the district general hospital setting where ancillary cytological facilities are not routinely available. The use of USCR may help reduce the need for diagnostic surgical biopsy and thereby facilitate referral to the appropriate clinical team.

References


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4.7 Howlett D C, Menezes L J, Lewis K, Moody A B, Violaris N, Williams M D
Sonographically Guided Core Biopsy of a Parotid Mass
American Journal of Roentgenology 2007; 168: 223-227
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Subject: David Howlett- PhD by publication.

Dear Anne


I am writing to confirm that David Howlett made a significant contribution to the above papers. David was responsible for study conception, design and interpretation. He critically revised the paper for important intellectual content and approved the final published version.

With best wishes.

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Sonographically Guided Core Biopsy of A Parotid Mass

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OBJECTIVE. The purpose of this study was to evaluate the accuracy of sonographically guided core biopsy in the evaluation of parotid masses.

SUBJECTS AND METHODS. Between 1998 and 2004, 135 patients consecutively presenting with a parotid mass were prospectively enrolled into this study. A single operator performed initial diagnostic sonography and then sonographically guided core biopsy using local anesthesia. Biopsy was performed with an 18- or 20-gauge needle and a spring-loaded biopsy gun with a mean of two passes per patient. Outcome measures were accuracy, sensitivity, specificity, and predictive values of sonographically guided core biopsy compared with the final pathologic diagnosis in the surgical group. In the nonsurgical group, final diagnosis was established on the basis of histologic findings after adequate core biopsy and clinical follow-up.

RESULTS. All sonographically guided core biopsy specimens were considered satisfactory for histologic evaluation. Overall, there were 71 benign tumors, 35 malignant tumors, and 29 inoperable, nonneoplastic lesions. In 76 (56%) of the 135 patients who underwent surgery, sonographically guided core biopsy and surgical histologic findings were correlated for 74 patients. In two cases sonographically guided core biopsy and surgical histologic findings did not correlate. In one case, the sonographically guided core biopsy finding was mucopapillary carcinoma, but the final diagnosis was squamous cell carcinoma. In the other case, the finding at sonographically guided core biopsy was squamous cell carcinoma, but the final diagnosis was mucoepidermoid carcinoma. The treatment of these patients was not affected. Fifty-nine (44%) of the 135 patients avoided surgery. In differentiation of benign from malignant disease, sonographically guided core biopsy had a sensitivity, specificity, and diagnostic accuracy of 100%. Sonographically guided core biopsy also had positive and negative predictive values of 100% in the diagnosis of malignancy. There were no significant complications of sonographically guided core biopsy.

CONCLUSION. Sonographically guided core biopsy is a highly accurate technique for evaluation of parotid lesions and can be safely performed as an outpatient procedure. Sonographically guided core biopsy has potential advantages over fine-needle aspiration cytologic examination, particularly in the typing and grading of lymphomas and carcinomas and in improved differentiation of reactive nodal hyperplasia from lymphoma. The use of sonographically guided core biopsy may help reduce the need for surgical biopsy and facilitate prompt referral to the appropriate clinical team.

Numerous pathologic processes present with parotid swelling, and it is frequently difficult on clinical grounds alone to determine whether the nature of a parotid mass. Reaching an accurate diagnosis when contemplating surgery is important, because many nonneoplastic and some neoplastic lesions may not require surgical intervention, particularly in patients at poor anesthetic risk. It also may be possible to manage certain benign neoplasms, such as Warthin's tumor, with minimal invasive surgical techniques such as extracapsular dissection. Accurate diagnosis is essential for selection of the appropriate operative procedure and to allow informed patient consent. After the fall from favor of open biopsy as the result of a high level of tumor seeding [1], fine-needle aspiration cytology (FNAC) has been widely adopted for assessment of parotid masses. High diagnostic accuracy has been found in some studies [2-6]. FNAC has well-documented limitations, however, and is frequently associated with high levels of inadequate or false-negative diagnoses [7, 8]. It is against this background that sonographically guided core biopsy of the parotid gland has been investigated [9-11]. Previous studies in-
Fig 1—32-year-old woman with normal parotid gland. Longitudinal sonogranates shows main intraparenchymal vessels. Fat stratum bulbaris clearer vascular area is superficial to external ear artery (small arrow). Face not shown because it is superficial to retroauricular skin. Deep parotid lobe (3) is deep in relation to plane passing through path of nerve, and superficial lobe (5) is superficial to this plane.

162/19, 84/10, and 53/11 patients with parotid swelling and showed a diagnostic accuracy of 97% [10, 11] to 100% [9] for sonographically guided core biopsy findings compared with surgical histologic findings, and there were no significant complications. In two of the studies [9, 10], 18-gauge or smaller needles were used with a mean of two passes per patient. In the third study [11], small- and large-bore needles (up to 14-gauge) and a range of needle passes were used. The purpose of our study was to evaluate the accuracy and safety of sonographically guided core biopsy performed with only small-bore needles in a series of 135 patients presenting with a parotid mass.

Subjects and Methods

Over the 7-year period from 1998 to 2004, 135 patients consecutively referred for evaluation of a parotid mass were incorporated into this prospective study. Sixty-three patients were men and 72 were women. The age range was 16-90 years (mean, 60 years). After initial diagnostic sonographic examination (ATL, HDI 5000 system, Philips Medical Systems) with a high-resolution linear array transducer (3-5 MHz; 7-4 MHz for larger patients or for deeper lesions), the operator proceeded to core biopsy. Before biopsy, written consent was obtained from the patient, and the benefits and potential hazards of the procedure were explained. Contraindications to biopsy included inability to provide written consent or to cooperate and concurrent use of anticoagulant medication or presence of known bleeding diathesis. Preprocedural assessment of platelet count and clotting parameters was not undertaken routinely. All diagnostic sonographic examinations and biopsies were performed by a single operator using a fixed biopsy technique. With an aseptic technique and after administration of 1% lidocaine local anesthetic, a small skin incision was made and a biopsy needle introduced under sonographic guidance. Biopsy specimens were obtained with a spring-loaded device. For the first 16 patients a 22-mm fixed-thrust mechanism (Biopsy Gun, Bard) was used; and thereafter, a 15- to 22-mm variable-thrust device (Magnum gun, Bard). An average of two passes were made per patient. Biopsy samples were fixed in a jar containing 10% formalin and were sent for histologic analysis.

All parotid lesions were deemed sonographically as lying in the superficial lobe of the gland and had a size range of 6-58 mm. In most (n = 122) of the patients, 18-gauge needles were used. Because of the borders of facial nerve and vascular injury, 20-gauge needles were used in patients (n = 13) with smaller lesions situated closer to the main parotid vessels. Under sonographic guidance, lesions were approached along the longitudinal, oblique, or transverse plane, depending on the position of the lesion and to avoid adjacent structures (Fig 1). Biopsy specimens of cystic lesions were obtained from the cyst wall, samples being directed at the more solid components of lesions of mixed cystic and solid appearance.

The needle throw of the variable-thrust biopsy device was selected according to the size and situation of the lesion to allow adequate lesion sampling but to ensure the needle did not exit deep in relation to the lesion (Fig 2). Most of the biopsy procedure took less than 15 minutes. After biopsy, patients were asked to compress the puncture site and were observed for 30 minutes before discharge.

Final diagnosis was established on the basis of adequate histologic findings in the core biopsy specimen and surgical histologic findings for the surgical group or clinical follow-up findings for patients who did not undergo surgery. The follow-up period ranged from a few months to 7 years.

Results

Of the 135 patients in the study, 76 underwent surgery and 59 avoided surgery. Initial sonograms showed focal lesions suitable for biopsy in 124 patients; 11 patients in the non-surgical group had diffuse sonographic abnormalities with no discrete focal lesion. All sonographically guided core biopsy specimens were considered satisfactory for evaluation by the histopathologist. In the surgical group, 55 patients had a diagnosis of benign neoplasms (37 pleomorphic adenomas [Fig 3]; 16 Warthin's tumor [Fig 4]; two, oncocytomas). Eighteen patients had a diagnosis of malignancy (three mucoepidermoid carcinomas [Fig 5]; one, adenoid cystic carci-
and no focal lesion found at sonography (six, fatty infiltration; one, Sjögren’s syndrome [Fig. 6]; one, sarcoidosis; two, chronic sialadenitis; one, normal parotid gland).

The patient with a core biopsy diagnosis of normal parotid tissue presented with bilateral parotid swelling. At sonography the glands appeared hypoechoic and enlarged, suggestive of fatty infiltration. Biopsy specimens were obtained from the superficial lobe of the right parotid gland. After a normal histology report, no further investigations were undertaken.

There was complete agreement between the results of sonographically guided core biopsy and surgical histologic findings in 74 of 76 patients. The two cases that did not correlate were malignant tumors. One of these tumors was diagnosed as squamous cell carcinoma at sonographically guided core biopsy, but the final histologic result was mucoepidermoid carcinoma. In the other case, the core biopsy was mucoepidermoid carcinoma, but the final histologic result was squamous cell carcinoma. The treatment of these two patients was not affected by these findings; both underwent surgical excision.

Only six of 17 patients with a core biopsy diagnosis of non-Hodgkin’s lymphoma needed surgical biopsy for further treatment information. The eight patients with reactive nodal hyperplasia diagnosed at sonographically guided core biopsy were well during clinical follow-up. Sixteen patients with benign neoplasms did not undergo surgical treatment. They either declined or were unfit for surgery and continued to undergo observation. Three nonneoplastic lesions were managed surgically either for symptom control or at patient request.

Sonographically guided core biopsy was well tolerated by all patients with no immediate complications. A small subcutaneous hematoma was present at surgery in one patient who had undergone biopsy of a Warthin’s tumor. The hematoma was in the soft tissue overlying the gland at the biopsy site and was impalpable. The patient had no predisposing risk factors for bleeding, and surgery was uneventful. No evidence of tumor seeding was detected during follow-up.

To assess the utility of sonographically guided core biopsy in the diagnosis of malignancy and to differentiate benign from malignant disease, we compared histologic results and sonographically guided core biopsy findings for the 76 patients who underwent both biopsy and surgery. There were 18 true-positive findings (malignant diagnosis and biopsy), 34 true-negative findings (benign diagnosis and no
false-positive or false-negative findings, giving sonographically guided core biopsy a sensitivity, specificity, and diagnostic accuracy of 100% and 100% positive and negative predictive values in the diagnosis of malignancy.

Discussion

FNAC as a technique has a number of advantages in assessment of parotid masses. It is fast, safe, well tolerated, and accurate when performed by skilled practitioners. The accuracy of FNAC can be enhanced within a specialist clinic, which may be led by a cytologist [3] or a radiologist [12]. Outside the specialist clinic, however, the accuracy of FNAC decreases significantly with acquisition of large numbers of aspirate samples that do not give enough information for diagnosis [7, 8]. Even when the procedure is performed by an experienced practitioner, they are well recognized pitfalls in the cytologic diagnosis of pleomorphic adenoma [13, 14] and Warthin’s tumor [15]. Despite the use of ancillary cytologic techniques (flow cytometry and in situ hybridization) with FNAC in the diagnosis of lymphoid proliferation, it is often difficult to differentiate low-grade lymphoma from reactive nodal hyperplasia [16], and FNAC of lymphoma is not generally considered definitive [17]. In these cases FNAC often acts as an indicator of the need for surgical biopsy. Differentiation of reactive atypia in benign squamous epithelium from well differentiated squamous cell carcinoma may not be possible with FNAC [18]. In addition, it is often not possible to diagnose parotid involvement by systemic disease such as Sjögren’s syndrome and sarcoidosis with FNAC or to accurately grade and type carcinomas and lymphomas or to differentiate in situ from invasive disease [10, 16]. FNAC has a low predictive value for benign neoplastic lesions [6], and a negative FNAC result has a low negative predictive value [5]. FNAC is more likely not to give enough information for diagnosis of small lesions, those of low cellularity, and those with inconclusive histologic features.

The pitfalls of FNAC have led some authors to study the use of sonographically guided core biopsy in assessment of parotid masses [9-11]. The combination of initial diagnostic sonography with biopsy is useful because the parotid glands are superficial structures, readily amenable to assessment with high-resolution sonography. Sonography is the initial imaging technique of choice for the characterization and delineation of parotid masses, and the findings can be used as a guide for additional imaging (usually MRI) of possibly malignant lesions and of lesions the full extent of which is difficult to see, in particular if there is deep lobe involvement, an area of sonographic weakness due to mandibular obscuration [19, 20]. The use of sonographic guidance for biopsy is important because it allows accurate needle placement, such that the needle traverses but does not exit deep in relation to the lesion and avoids adjacent structures. A variable tumor cell, the biopsy device is useful when space is confined. Some needle devices allow initial passage of the inner stylet for exact positioning of the needle tip, with subsequent discharge of the outer sheath over the fixed inner stylet to obtain a core of tissue. This technique may help reduce damage to deeper structures. Sonographic guidance also allows central sampling of a lesion with improved diagnostic yield [21], and necrotic areas can be bypassed. Sonography may also depict clinically inapparent disease.

In our study, sonographically guided core biopsy had a diagnostic accuracy of 100% in the surgical group, comparable with previous findings. Sonographically guided core biopsy also had 100% sensitivity and specificity in the differentiation of benign from malignant disease and 100% positive and negative predictive values in the diagnosis of malignancy. There was no correlation between sonographically guided core biopsy findings and surgical histologic findings in only two cases, of mucoepidermoid and squamous cell carcinoma, but management was unaffected. In all cases, biopsy specimens with which a diagnosis could be determined were obtained with small-bore needles (18-20-gauge) with an average of two passes per patient. Sonographically guided core biopsy was well tolerated with no significant complications. Unlike FNAC, sonographically guided core biopsy requires formal histologic reporting, which is time-consuming, and it is more invasive than FNAC, requiring local anesthesia and a skin incision.

The main advantage of core biopsy over FNAC is that a core of tissue is obtained that can be used for formal histologic and immunohistochemical analysis. This advantage improves differentiation of low-grade lymphoma from reactive nodal hyperplasia, allows grading and typing of lymphoma and poorly differentiated carcinoma, and helps determine the likely origin of metastatic carcinoma. In our study only six (33%) of 17 patients with non-Hodgkin’s lymphoma needed surgical biopsy for additional treatment information, and no patient with a core biopsy diagnosis of reactive nodal hyperplasia underwent surgical excision, eliminating any uncertainty. Eleven patients were excised for whom a focal lesion was detected with sonography, and sonographically guided core biopsy for evaluation of possible parotid involvement by systemic disease.

Although there were no major complications of sonographically guided core biopsy in our study, there are hazards of core biopsy that need to be considered, including hoarseness, facial nerve injury, and tumor seeding. The parotid and submandibular vein and external carotid artery are major intraparotid vessels; they are well visualized with sonography (Fig. 1) and can be avoided [20]. The facial nerve is not readily identified with sonography, although its position can be inferred because the nerve passes in a plane superficial to the retromandibular vein and can be avoided [14, 20].

Tumor seeding along the needle track is a hazard of both FNAC and core biopsy. The risk of tumor seeding varies according to the organ involved and the site of the needle used. Tumor seeding is described in as many as 12% of cases of FNAC of thoracic esophagus [22], with an incidence of 0.02% for abdominal tumors [20]. Tumor seeding tends to occur with larger-bore needles, probably because these needles allow aspiration of serotoneural fragments and allow tumor cells to pass through the needle tract, although this approach has not been adopted at our institution. Although there was no evidence of tumor seeding in our study population, patient follow-up was limited to only a few months in some cases, and continued surveillance is needed.

In conclusion, sonographically guided core biopsy is a highly accurate, safe, and well-established technique for the diagnosis of parotid masses. The procedure can be performed with small-bore needles on an outpatient basis. Sonographically guided core biopsy has advantages over FNAC, particularly in differentiation of lymphoma from reactive nodal hyperplasia, in typing and grading of carcinoma and lymphoma, and in the assessment of parotid involvement by systemic disease. The use of sonographically guided core biopsy may reduce the high rate of surgical biopsy associated with FNAC that does not provide enough information for diagnosis and may facilitate both prompt referral to the relevant
clinical team and selection of an appropriate operative procedure if needed.

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References
Breeze J, Andi A, Williams M D, Howlett D C

The Use of Fine Needle Core Biopsy Under Ultrasound Guidance in the Diagnosis of a Parotid Mass

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Subject: David Howlett - PhD by publication

Dear Anne

Re: Breeze J, Andi A, Williams MD, Howlett D C


I am writing to confirm that David Howlett made a significant contribution to the above paper. David was responsible for study conception and design and was significantly involved in data analysis and interpretation having acquired the study data. He critically revised the paper for important intellectual content and was involved in final approval of the final published version.

With best wishes,

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Technical note

The use of fine needle core biopsy under ultrasound guidance in the diagnosis of a parotid mass

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Keywords: Parotid Neoplasia; Ultrasound; Core Biopsy

We aimed to evaluate data about the performance of ultrasound-guided core biopsy (USCB) in the diagnosis of parotid swellings and to supplement previous studies in this area. Sixty-five patients were enrolled in this prospective study in addition to our previously published series of 135 patients1 with follow-up periods ranging from a few months to nine years. The technique of initial diagnostic ultrasound and characterisation of the lesion followed by guided core biopsy is identical to that previously described.1,2 Using a spring-loaded automated and variable flow biopsy device and a combination of 18 or 20G needles (mean of two passes/patient).

In the previous series all core biopsies were considered sufficient for histological analysis and there were no false positive or false negative results. Of 200 patients in the updated series, 116 were operated on subsequently (Table 1) and 84 patients were not (Table 2). Two core biopsy specimens in the additional study group of 65 patients had non-diagnostic core biopsy samples and there was also a single false negative result.

In the two patients in whom USCB was not diagnostic, both lesions had prominent cystic and necrotic internal components as shown on the initial diagnostic ultrasound scan. Despite sampling of the solid elements, core biopsy samples were inadequate for diagnosis. Ultrasound scans had suggested possible diagnoses of Warthin tumour in one case and malignancy in the other. The final histological examination confirmed Warthin tumour and adenocarcinoma, respectively.

In the false negative case the patient presented with a lesion of the superficial lobe that looked clinically and sonographically malignant. He had an initial non-guided fine-needle aspiration biopsy, which showed a probable pleomorphic adenoma, but was sent for USCB because of the clinical findings. USCB sampled the lesion at several levels, and the histological picture was reported as a basal cell adenoma. The lesion was excised and found to be a well-differentiated basal cell adenocarcinoma. Core biopsy specimens were reviewed and contained only samples from the centre of the lesion with no encapsular components.

It is accepted that well-differentiated adenocarcinomas can be histologically indistinguishable from benign adenomas unless there is capsular involvement to indicate malignancy. It is not dissimilar from follicular lesions in the thyroid, and often final diagnosis can be made only when the whole lesion is excised and can be examined histologically. USCB sampling of the periphery of the lesion as well as the core may help to reduce this, but capsular infiltration may be patchy, clinical and other imaging should allow appropriate treatment in these rare cases. The non-diagnostic and false negative results of core biopsy illustrate potential weaknesses of USCB that are more widely associated with fine needle aspiration cytology.

During the clinical follow-up period of the 200 patients there have been no documented cases of tumour recurrence to date. Two small haematomas after biopsy developed in
the additional group of patients, neither of which required treatment. Twenty-two patients had lymphoma diagnosed by core biopsy, 12 of whom had sufficient information obtained from USCB alone to allow definitive treatment.

The increasing acceptance of USCB as a technique by haematologists and oncologists may reduce the need for excisional biopsy. At this stage we have not formally compared initial diagnostic ultrasound with subsequent core biopsy diagnosis to assess correlation and whether USCB changed management, but this may form the basis of a future study.

Overall of the 198/200 patients whose core biopsies were considered suitable for diagnosis, the technique had an accuracy of 99.1%, a sensitivity of 96.8%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 98.8%. USCB remains a safe and accurate method for diagnosing parotid lesions. Some lesions may prove challenging for USCB, particularly those that are highly necrotic, but correction with clinical findings and imaging should allow appropriate treatment. The high negative predictive value of USCB will facilitate the use of minimally invasive techniques for parotid surgery, such as extracapsular dissection.

### Acknowledgements

The authors would also like to acknowledge Mr Andrew Moody, Mr George Mankiny, Mr Keith Allman and Mr Nick Violanis for their contribution.

### References


Evaluation of Biopsy Methods in the Diagnosis of Submandibular Space Pathology

A.Mandy@brighton.ac.uk

Re: David Howlett: PhD by Publication

Dear Anne


I am writing to confirm that David Howlett made a significant contribution to the above paper. David was largely responsible for study conception and design, assisted with data acquisition, analysis and interpretation and was also heavily involved in critical revision of the final version for intellectual content and the final approval of the version to be published.

With best wishes.

Yours sincerely

[Signature]

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Evaluation of biopsy methods in the diagnosis of submandibular space pathology


Abstract. The aim of this study was to evaluate the performance of fine needle aspiration cytology (FNAC), ultrasound-guided core needle biopsy (USCNB), punch biopsy, and surgical excision biopsy in neoplasms present within the submandibular space. A retrospective analysis of all patients with a pathological diagnosis of a submandibular space neoplasm within a 12-year period (February 1999 to June 2011) was performed. Biopsy results were compared to histopathological diagnosis obtained from surgical excision biopsy. Eighty-one specimens from 45 patients met the search criteria (15 FNAC, 24 USCNB, 7 punch biopsy, and 35 surgical excision biopsy). The final diagnosis was established by USCNB, punch biopsy, or surgical excision biopsy and not by FNAC alone. Surgical excision biopsy was performed as a primary diagnostic (n = 15), or as a post-diagnostic therapeutic procedure (n = 12). Non-diagnostic results were: FNAC 11/15, USCNB 2/24, and punch biopsy 17. Diagnostic results were: FNAC 3/15, USCNB 20/24, and punch biopsy 5/7. No complications were reported. Although punch biopsy demonstrated good yield and accuracy, its use is restricted to a small cohort of patients. USCNB is a safe and accurate technique in the submandibular space, with a low non-diagnostic rate.

The salivary glands comprise three paired major glands (parotid, submandibular, and sublingual glands) and 600–1000 minor glands distributed widely beneath the mucosa of the oral cavity, palate, parotid, and sublingual spaces, and upper respiratory tract. Approximately 6% of all head and neck tumours occur within the salivary glands; 80% of these occur within the parotid gland, 10–15% within the submandibular gland, and the remaining 5–10% within the sublingual and minor salivary glands. Approximately 50% of submandibular gland neoplasms are benign, with pleomorphic adenoma accounting for over 90% of them. 50% are malignant, with adenoid cystic carcinomas being the most common, accounting for 85% of cases. Controversy remains regarding the best biopsy method for salivary gland neoplasms, with very little published data pertaining to the submandibular gland and submandibular space. However, accurate diagnosis is needed to guide appropriate management and avoid unnecessary surgical intervention. Historically, fine needle aspiration cytology (FNAC) has been the main biopsy method in the salivary glands; it is safe, quick to perform, and well suited to an outpatient setting. It has a high specificity in the head and neck (98%), but a relatively low false-negative rate and variable diagnostic accuracy (66–90%). It requires optimized circumstances to perform well, including ultrasound guidance and a cytologist.
present at the time of sampling. These findings are not widely available leading to reported heterogeneity in performance across various centres. The lack of consistency in terms of FNAC sensitivity and diagnostic accuracy has led to the increasing use of alternative methods such as ultrasound-guided core needle biopsy (USCNB) and punch biopsy. Ultrasound provides good anatomical and pathological characterization, therefore biopsies can be performed safely under direct visualization without damaging neighbouring structures. The increase in ultrasound expertise and image quality among radiologists and clinicians who utilize it regularly has had a direct effect on the use of ultrasound-guided biopsy methods, such as ultrasound-guided FNAC and USCNB, with improved diagnostic accuracy and less variability in performance compared to blind FNAC. Punch biopsy is a more invasive biopsy method suitable for superficially located lesions. There is a paucity of data looking at the performance of these biopsy methods for submandibular space neoplasms. The aim of this study was to evaluate the diagnostic performance of FNAC, punch biopsy, and USCNB in the diagnosis of lesions of the submandibular space.

Materials and methods

The pathology database (APEX) was reviewed to identify all patients who underwent a submandibular gland/space biopsy within a 12-year period (February 1999 and June 2011). All patients with a pathological diagnosis of submandibular gland/space neoplasms were included in the study. If a surgical excision biopsy was undertaken (diagnostic or therapeutic), the histology result was used as the reference standard. Clinical records, radiology and pathology reports, and PACS (Picture Archiving and Communication Systems) imaging were reviewed in each case. The following details were collated from the pathology database: (1) date and anatomical site of biopsy, (2) biopsy technique (FNAC, USCNB, punch biopsy, or surgical excision biopsy); (3) needle gauge and number of biopsy passes; (4) adequacy of biopsy specimen; (5) relevant previous pathology and final biopsy results.

FNAC

All FNAC were performed blind in the outpatient setting (ENT or maxillofacial surgery clinic) by a range of clinicians. A 21-gauge needle was routinely employed without the administration of a local anaesthetic. A cytologist was not present in the outpatient clinic for immediate sample analysis.

USCNB

USCNB were performed by consultant radiologists within the radiology department. A diagnostic ultrasound was routinely performed prior to biopsy, with written consent. Two to five millilitres of 1% lignocaine was infiltrated into the submandibular gland prior to making a small skin incision. The biopsy was performed using a technique similar to that described previously in parotid neoplasms, with a spring-loaded semi-automatic biopsy gun and variable throw 18/20-gauge needle (Bard Magnum; C. R. Bard Inc., Covington, GA, USA).

Punch biopsy

Punch biopsies were performed by maxillofacial or ENT surgeons in a day surgery unit, with local anaesthesia, using 1–8 mm circular blades to produce cylindrical cores of tissue.

Definitions

For the purpose of this study the following terms are defined: (1) Diagnostic specimen: a specimen that yielded a single definitive cytological or histological diagnosis; (2) 'Non-diagnostic' specimen: a specimen that did not yield a single definitive cytological or histological diagnosis; these were subdivided into insufficient or equivocal samples. The non-diagnostic rate was calculated from the insufficient samples, as equivocal results did provide some useful information to guide management, although they were not truly diagnostic. (3) 'Primary diagnostic surgical excision': a surgical excision performed prior to any prior or subsequent FNAC/USCNB/punch biopsy; (4) 'Secondary diagnostic surgical excision': a surgical excision performed after initial non-diagnostic FNAC/USCNB/punch biopsy; (5) 'Therapeutic surgical excision': a surgical excision performed for therapeutic purposes after cytological/histological diagnosis was established from prior FNAC/USCNB/punch biopsy.

Results

A total of 81 specimens from the submandibular gland/space met the inclusion criteria and were analysed. Each FNAC/USCNB/punch biopsy was treated as a separate episode for the purpose of the study. There were 44 patients: 22 males and 22 females. The age range was 23–98 years, with a mean of 66 years.

FNAC

Fifteen FNAC were performed in 13 patients; two patients underwent repeat FNAC due to the initial samples being inadequate for analysis (Table 1). Of the

<table>
<thead>
<tr>
<th>Patient</th>
<th>FNAC</th>
<th>USCNB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Pleomorphic adenoma</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Epithelial T lymphoma or reactive node</td>
<td>MALT B-cell lymphoma</td>
</tr>
<tr>
<td>8</td>
<td>Epithelial T lymphoma or reactive node</td>
<td>MALT B-cell lymphoma</td>
</tr>
<tr>
<td>9</td>
<td>Low grade B-cell lymphoma (secondary)</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>Non-diagnostic (insufficient tissue)</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>Pleomorphic adenoma</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>High grade B-cell lymphoma (secondary)</td>
<td>-</td>
</tr>
</tbody>
</table>

FNAC, fine needle aspiration cytology; USCNB, ultrasound-guided core needle biopsy; MALT, mucosa-associated lymphoid tissue.
### Table 2. Ultrasound-guided core needle biopsy: 13 patients, 24 episodes.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Initial USCBN</th>
<th>Surgical excision (primary, secondary or therapeutic)</th>
<th>USCBN episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pleomorphic adenoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>MALT B-cell lymphoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>High-grade B-cell lymphoma</td>
<td>High grade B-cell lymphoma (therapeutic)</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>B-cell lymphoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>5-7</td>
<td>Pleomorphic adenoma</td>
<td>Pleomorphic adenoma (therapeutic)</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>Warthin's tumour</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>MALT lymphoma</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>MALT lymphoma (repeat)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>Pleomorphic adenoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>Metastatic squamous cell carcinoma</td>
<td>Metastatic squamous cell carcinoma (therapeutic)</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>Squamous cell carcinoma</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>Melanoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Non-diagnostic tissue (minor salivary gland tissue only)</td>
<td>Plasmocyte adenoma (secondary)</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>Non-diagnostic (inflammatory tissue only)</td>
<td>Low grade adenocarcinoma (secondary)</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>Epithelial (neoplastic, metastatic/Warthin's tumour)</td>
<td>Ductal cyst (secondary)</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>Epithelial (? pleomorphic adenoma/adenoacanthoma)</td>
<td>Adenocarcinoma (secondary)</td>
<td>1</td>
</tr>
</tbody>
</table>

*Presented on three further occasions with separate lumps that yielded MALT lymphoma.

USCBN, ultrasound-guided core needle biopsy; MALT, mucosa-associated lymphoid tissue.

18 patients, three subsequently underwent USCBN and 14 underwent a surgical excision biopsy; one patient had both FNAC and USCBN. Thirteen FNAC samples were non-diagnostic due to either an insufficient amount of tissue sample (n = 11) or equivocal results (n = 2). The insufficient samples eventually yielded pleomorphic adenoma (n = 6). Warthin's tumour (n = 1), lymphoma (n = 3), and squamous cell carcinoma (n = 1). Two FNAC samples yielded pleomorphic adenoma that correlated with subsequent USCBN or surgical excision biopsy. Nine secondary diagnostic surgical excisions and two therapeutic surgical excisions were performed.

### USCBN

Twenty-four USCBN were performed in 18 patients (Table 2). A repeat USCBN was performed in three patients following initial USCBN; these yielded B-cell lymphoma, mucosa-associated lymphoid tissue (MALT) lymphoma, and squamous cell carcinoma. Patient 9 re-presented with new lumps in three further episodes, with USCBN confirming recurrent MALT lymphoma in each episode, resulting in a total of 24 USCBN. Four USCBN were non-diagnostic due to insufficient tissue (n = 2) and equivocal results (n = 2). Twenty USCBN were diagnostic yielding pleomorphic adenoma, lymphoma, Warthin's tumour, myoepithelial carcinoma, squamous cell carcinoma, and melanoma (Table 2). Six therapeutic surgical excisions and four secondary diagnostic surgical excisions were performed. All six therapeutic surgical excisions correlated with the initial USCBN. USCBN were performed with an 18-gauge needle with an average of two passes (range 1–4).

#### Punch biopsy

Seven punch biopsies were performed in seven patients (Table 2). Two punch biopsies were non-diagnostic due to insufficient tissue sample (n = 1) and equivocal result (n = 1). Five punch biopsies yielded adenocarcinoma, canalicular adenoma, adenoid cystic carcinoma, and pleomorphic adenoma. Four therapeutic surgical excisions and two secondary diagnostic surgical excisions were performed. All four therapeutic surgical excisions correlated with the initial punch biopsy.

### Diagnosis from non-surgical biopsy alone

USCBN or punch biopsy alone was used to establish the final diagnosis in nine patients. USCBN yielded lymphoma (n = 3), pleomorphic adenoma (n = 2), Warthin's tumour (n = 1), squamous cell carcinoma (n = 1), and melanoma (n = 1). Punch biopsy yielded canalicular adenoma (n = 1).

### Surgical excisions

Thirty-five surgical excision biopsies were performed: eight primary diagnostic surgical excisions, 15 secondary diagnostic surgical excisions, and 12 therapeutic surgical excisions. There were eight patients who underwent surgical excision with no preoperative biopsy diagnosis (pleomorphic adenoma (n = 3), canalicular adenoma (n = 1), lipoma (n = 1), myoepithelium

### Table 3. Punch biopsy: seven patients, seven episodes.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Punch biopsy</th>
<th>Surgical excision (primary, secondary or therapeutic)</th>
<th>Punch biopsy episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Adenocarcinoma</td>
<td>Adenocarcinoma (therapeutic)</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Canalicular adenoma</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>3, 4</td>
<td>Adenoid cystic carcinoma</td>
<td>Adenoid cystic carcinoma (therapeutic)</td>
<td>2</td>
</tr>
<tr>
<td>5, 6</td>
<td>Pleomorphic adenoma</td>
<td>Pleomorphic adenoma (therapeutic)</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Epithelial (? pleomorphic adenoma or adenocarcinoma)</td>
<td>Adenocarcinoma (secondary)</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>Non-diagnostic tissue (insufficient tissue)</td>
<td>Warthin's tumour (secondary)</td>
<td>1</td>
</tr>
</tbody>
</table>

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(n = 1), squamous cell carcinoma (n = 1), and adenocarcinoma (n = 13). Three non-diagnostic FNAC yielded malignant lesions at surgery (lymphoma (n = 2) and adenocarcinoma of unknown origin (n = 1)) and one non-diagnostic USCNB yielded adenocarcinoma.

Non-diagnostic results
Non-diagnostic rates were calculated from specimens that did not yield a single definitive cytological or histopathological result, i.e., insufficient samples (equivocal results with two or more suspected diagnoses) were excluded because they provided some diagnostic information, albeit inconclusive. Results showed non-diagnostic rates of: FNAC 79% (1/15), USCNB 8% (2/26), and punch biopsy 14% (1/7).

Diagnostic results
The overall analysis of diagnostic specimens yielded 27 benign (56%) and 21 malignant (44%) lesions. Pleomorphic adenomas accounted for 46% (10/22) of all the lesions and 70% (19/27) of the benign tumours. Mucoepidermoid carcinoma accounted for 6% (3/58). Canalicular adenoma, ductal cysts, myoepitheliomas, oncocytomas, and lipomas each accounted for 2% (1/48).

Lymphomas were the most common malignant tumours, accounting for 19% (6/34) of all the lesions and 43% (9/21) of the malignant tumours. Adenoid cystic carcinoma, adenomucinosa, and squamous cell carcinomas each accounted for 6% (3/58). Acinic cell carcinoma, myoepithelial carcinoma, and melanomas each accounted for 2% (1/48).

Discussion
The majority of studies evaluating biopsy methods for salivary gland neoplasms are centered on the parotid gland, with few studies evaluating the submandibular, sublingual, and minor salivary glands. To the best of our knowledge, this study represents the largest reported submandibular biopsy series with 81 biopsy specimens. For submandibular gland neoplasms, as with the parotid gland, triple assessment, namely clinical examination, imaging, and pathological diagnosis, is imperative for accurate preoperative diagnosis, treatment planning, counselling, and prognostic purposes. Cell/tissue can be obtained from the submandibular space via FNAC, USCNB, punch biopsy, or surgical excision biopsy for pathological analysis, with each technique having varying advantages and disadvantages. FNAC is simple, quick to perform, minimally invasive, and has been the traditional biopsy method of choice in the major salivary glands. There is however significant variability in its performance and diagnostic accuracy across various institutions, dependent upon operator experience, use of ultrasound guidance, adequacy of sample, interpretative skills, on-site presence of a cytologist, and finally availability of ancillary methods such as flow cytometry for additional analysis. Ultrasound-guided FNAC improves tissue yield and can be associated with a high agreement (95%) with surgical excision biopsy results, comparable to 95-97% accuracy reported for USCNB. An insufficient amount of cellular aspirate is often obtained in 2-15% of cases, also a high false-negative rate has been reported across a wide range of studies. Therefore, the high specificity (98%) and sensitivity (80%) reported in some centres is not generally reproducible where the circumstances for FNAC are not optimized. FNAC also cannot reliably differentiate low-grade lymphomas from reactive nodal hyperplasia and in most cases acts as an indicator for the need for an excision or other biopsy technique.

In our series, two equivocal FNAC specimens yielded MALT B-cell and low-grade B-cell lymphomas on subsequent USCNB and surgical excision, respectively (Table 1). Hern et al. illustrated that despite the recommended National Institute for Health and Clinical Excellence (NICE) model of a one-stop head and neck clinic with an loco-regional radiologist performing ultrasound-guided FNAC and cytologists analysing samples, the practicalities of implementing the recommendation outside of large specialist units is difficult and rarely achieved. The high non-diagnostic rates (73%) for FNAC in our series is likely due to a combination of small sample size (n = 15), lack of optimization due to variability in the skills and experience of the operators, and lack of imaging guidance or on-site cytologist. It was observed that from clinicians, despite performing FNAC, requested additional USCNB probably to争取 satisfaction of a non-diagnostic FNAC specimen.

Frozen section is another biopsy technique that has consistently performed better than FNAC in the evaluation of parotid gland lesions, with a higher sensitivity (95% vs. 80%) and specificity (99% vs. 97%). Archival features such as capsular and perineural invasion are preserved, therefore improving its overall accuracy. It can be used to clarify the non-diagnostic results and allows accurate margin evaluation. In our series there is little data on its performance in the submandibular gland and it requires an on-site pathologist for immediate evaluation. Due to the complexity of submandibular gland pathology, trying to reach an immediate diagnosis from frozen sections is unlikely to be feasible outside of specialized units.

USCNB has the advantage that it provides a core of tissue with preserved glandular and malignant cells of lymphoid proliferation. With a larger tissue core, capsule invasion can be assessed, potentially enabling differentiation of adenoid cystic carcinoma from other forms of micro-morphologic adenomas. Several studies evaluating USCNB for parotid gland neoplasms have reported a high sensitivity (93-100%) and specificity (100%). It is more accurate, less heterogeneous in performance, and is associated with lower complication rates than FNAC. There was correlation in definitive diagnosis between USCNB and surgical excision in two of 24 specimens (8.3%). USCNB is not without disadvantages; it is more invasive than FNAC and tends to be associated with a lower success rate (usualy bi- to quad-gauge needle). However, due to minor bleeding is documented in 1-2% of cases in the parotid gland, however there are no reports of major complications or death in this or other studies evaluating the procedure. Tumour seeding is an uncommon complication with only two reported cases in the parotid gland. It appears to be related to tumour type, site of puncture, and increasing needle diameter, it is not described with Bi- or smaller needles. USCNB is superior to ultrasound-guided FNAC in diagnosing malignant lesions of the parotid gland with higher sensitivity (94.1% vs. 55.6%), specificity (100% vs. 93.5%), and accuracy (98.4% vs. 79%). FNAC probably in not series, USCNB has been used as an alternative diagnostic tool in two patients following prior non-diagnostic FNAC and is the only diagnostic tool in seven patients, avoiding surgical intervention in all nine patients. The movement towards the use of USCNB as the primary method of sampling in triple assessment of salivary gland lesions has been a result of consistent reports of high levels of
accuracy in diagnosing malignancy in parotid gland lesions, low false-negative and also low false-positive rates, coupled with low complications and good patient acceptability; 77.20). However, it takes time for units to accept and understand the role of USCNB, particularly pathologists who may not be used to interpreting these specimens.

Our study does have limitations. Submandibular gland neoplasms are uncommon compared to parotid gland neoplasms, hence the limited data in the published literature and the relatively small number in this study over a 12-year period. This lack of data for submandibular gland neoplasms makes it difficult to reliably ascertain the diagnostic accuracy and performance of these biopsy techniques for submandibular gland neoplasms, unlike in the parotid gland. In this study, FNAC was not performed under optimized circumstances, making accurate comparisons with other biopsy techniques difficult; however, the data obtained for blind FNAC are likely to reflect clinical practice in many units.

It was also difficult in many cases to ascertain with confidence the exact location of lesions within the submandibular space despite correlation with histology reports.

Although submandibular gland neoplasms are uncommon compared to those of the parotid gland, accurate diagnosis remains essential for appropriate management. In this study, USCNB performed well, as did punch biopsy in a selected patient group, with a high correlation following surgical excision biopsy and low non-diagnostic rate. It is unclear why the non-diagnostic rate for USCNB is higher for the submandibular gland compared to the parotid gland as reported in various studies. USCNB appears to be the preferred method of choice for submandibular gland space neoplasms, with a low non-diagnostic rate and also the ability to reliably differentiate lymphomas from benign nodal hyperplasia. The role of punch biopsy in the diagnosis of submandibular gland lesions is somewhat more ambiguous; punch biopsy is visible in a specific subset of participants with anatomically superficial lesions.

Ethical approval

Not required.

References


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4.10 Haldar S, Mandalia U, Skelton E, Chow V, Tighe D, Ramesar K,
Williams M D, Howlett D C

Diagnostic Investigation of Parotid Neoplasms – a 16 Year Experience of
Freehand Fine Needle Aspiration Cytology and Ultrasound Guided Core
Needle Biopsy

A. Mandy@brighton.ac.uk

Subject: David Howlett - PhD by Publication

Dear Anne

Re: Haldar S, Mandalia U, Skelton E, Tighe D, Ramesar K, Williams M, Howlett DC

Diagnostic Investigation of parotid neoplasms – a 16 year experience of fine-needle aspiration cytology and ultrasound guided core needle biopsy.

Accepted for publication, International Journal of Oral and Maxillofacial Surgery, June 2014.

I am writing to confirm that David Howlett made a significant contribution to the above paper. David was responsible for study conception and design together with data acquisition, he assisted with data analysis and interpretation together with critical revision of the paper for important intellectual content and final approval of the published version.

With best wishes,

Sananda Haldar

DR Sananda Haldar

Dear Sandi, can you fill in your current employment details, qualifications and contact details here please.

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STP 3 Clinical Radiology
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MBBS 2008
BS Anatomy 2007

Flat 8, 21 Cheesman Place
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Diagnostic investigation of parotid neoplasms: a 16-year experience of freehand fine needle aspiration cytology and ultrasound-guided core needle biopsy


Department of Radiology, Eastbourne District General Hospital, Eastbourne, East Sussex, UK

Abstract. This study aimed to examine the diagnostic yield of fine needle aspiration cytology (FNAC) and ultrasound-guided core needle biopsy (USCB) in the diagnosis of parotid neoplasia. A 16-year retrospective analysis was performed of patients entered into our pathology database with a final diagnosis of parotid neoplasia. FNAC and USCB data were compared to surgical excision where available. One hundred and twenty FNAC, 313 USCB, and 259 surgical specimens were analyzed from 397 patients. Fifty-six percent of FNAC and 4% of USCB were non-diagnostic. One hundred and thirty-two (33%) patients had a final diagnosis made by USCB and did not undergo surgery. Surgery was performed in 257 (65%) patients, 226 (88%) of whom had a preoperative biopsy. Most lesions were benign, but there were 62 parotid and 13 haematological malignancies diagnosed; false-negative results were obtained in three FNAC and two USCB samples. The sensitivity and specificity of FNAC were 70% and 89%, respectively, and for USCB were 93% and 100%, respectively. This study represents the largest series of patients with a parotid neoplasm undergoing USCB for diagnosis. USCB is highly accurate with a low non-diagnostic rate and should be considered an integral part of parotid assessment.

Key words: parotid neoplasm, ultrasound-guided core biopsy, fine needle aspiration cytology.

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A swelling in the parotid region provides a diagnostic challenge. The spectrum of pathologies presenting as a parotid mass is wide and it is not possible to visualize the benign and malignant, as well as the non-neoplastic lesions on clinical grounds alone. An accurate preoperative diagnosis of a parotid lesion is essential as surgery may be avoided in certain benign neoplasms and in many non-neoplastic lesions. Where the FNAC is considered too cautious or uninformative as a surgical decision tool, a biopsy is recommended. Core biopsy alone can provide sufficient tissue for grading and grading of malignant parotid tumors, including lymphoma, thus avoiding diagnostic surgical excision biopsy. Where surgery is required for therapeutic planning, notably with the increased use of extracapsular or parotid-sparring dissection, and to allow appropriate informed patient consent (in particular pertaining to facial nerve integrity and also possible nodal dissection in malignancy).

Open surgical excision biopsy (SEB), as a method of obtaining histological samples, remains the gold standard of reference. However, this reflects a high specificity in optimized circumstances, but has lower sensitivity, 15, 16; thus the false-negative biopsy results are being increasingly considered clinically unacceptable. ultrasound-guided core biopsy (USCB) has been described recently in the diagnosis of parotid tumors and is developing into an established technique. 17, 18 Controversy remains, however, regarding the optimal method for obtaining a tissue diagnosis. This study aimed to evaluate the utilization and performance of clinicians-performed non-guided FNAC and USCB in the diagnosis of parotid neoplasms over a 16-year period in a district general hospital.

Materials and methods

Ethical exemption was granted for the study; approval was not required for this retrospective study at our centre. Patients were identified from the pathology database for a 16-year period (March 1997 to June 2013). Specimens were entered into the APHP pathology database (medical database software) using specific systematic nomenclature of malignancy (SNOOD) topography and morphology codes for salivary gland neoplasms. All patients with a pathological diagnosis of parotid neoplasms were included in the study. If a preoperative biopsy was performed, the results of the biopsy (FNAC and/or USCB) were compared with the surgical specimen as reference standard. If surgery was not performed, the results obtained from USCB or FNAC would constitute the final diagnosis. Patients were retrieved using the specific coding parameters for salivary gland neoplasms and lymphomas as search criteria; all parotid neoplasms were selected. Non-neoplastic parotid lesions and xeroderma pigmentosum were excluded. Once histology reports were identified, the patients’ clinical notes were reviewed, and subsequent histology profiles were interrogated, and correlation was also made with patient records, radiology reports, and images from PACS (picture archiving and communication system).

The following data items were collated from the histology reports: (1) site and date of the biopsy; (2) For each sample, the pathologist used to provide the histological diagnosis was documented (i.e. FNAC, USCB, or SEB). (3) Needle gauge for USCB and the number of passes/samples. (4) For each patient, all relevant samples were collated for comparison (i.e. FNAC vs. USCB vs. SEB where available). A 21-gauge needle was used without the need for local anesthetic. The number of passes for FNAC was not recorded. Neither a cytopathologist nor a technician was present in the clinic at the time of sampling. All USCB were carried out in the hospital radiology department where patients underwent an initial diagnostic ultrasound and would then proceed to biopsy, if indicated. The majority of USCB (n = 560) were performed using an 18-gauge (1.2-mm) needle; the remainder (n = 7) were performed using a 20-gauge (1.6-mm) needle. USCB was performed using an automated biopsy device with a variable traverse facility of 15–22 mm (Magen Gun; Bard, Covington, GA, USA), using the technique described previously. 15 Standard calculations to determine the sensitivity, specificity, and accuracy of FNAC and USCB were then performed. For statistical analysis, the FNAC-USCB diagnosis was compared with the final surgical histological diagnosis, with surgery considered the reference standard. Non-diagnostic results were excluded from the analysis.

Also evaluated were the results of FNAC and USCB in patients who had both procedures during investigation of the same lesion. Actual findings following non-diagnostic FNAC and USCB were available, the number of cases with more than one FNAC or USCB during the work-up of the tumor, and the number of cases operated on with no firm preoperative diagnosis. We analyzed how often a diagnosis of malignancy was available preoperatively and the performance of USCB and FNAC in the diagnosis of haematological malignancy (i.e. how many cases were diagnosed and treated on the results of USCB or FNAC alone and how many required subsequent surgical excision for a precise diagnosis).

Definitions

A non-diagnostic biopsy result was defined as a biopsy where definitive cytopathology/histology was not obtained. Also, a diagnostic biopsy result was defined as a biopsy where no firm diagnosis was reached, where the pathology report was equivocal (e.g., fibrotic reactive lymph node or low-grade lymphoma) or where no representative tissue was obtained by biopsy. A false-negative biopsy result was one where histological indicated benign disease but the final surgical diagnosis was confirmed malignant. A false-positive biopsy result was one where histology indicated malignant disease but the final surgical diagnosis obtained at surgery was confirmed benign disease. A true-negative biopsy result was one where histology indicated benign disease and this was confirmed on final surgical diagnosis. A true-positive biopsy result was one where histology indicated malignant neoplasm and this was confirmed on final surgical diagnosis. A therapeutic excision was one where a histological diagnosis, from biopsy, was available prior to surgery and subsequent surgery was performed for therapeutic purposes. A primary diagnostic surgical excision was a surgical excision without any preoperative biopsy being performed. In this circumstance, surgery was performed for diagnosis and for treatment. A secondary diagnostic surgical excision was a surgical excision performed when a prior sample from FNAC/USCB had been non-diagnostic.
**Results**

There were 200 female and 197 male patients with an age range of 24–164 years (mean age 67 years). A primary diagnostic surgical excision was performed in 31 patients (7.8%). Of the 397 patients, 305 had USCB and 110 had FNAC. Eight repeat USCB and 10 repeat FNAC were undertaken, giving a total of 33 USCB and 120 FNAC. Surgery was performed in a total of 257 patients (excluding the 21 primary excisions); two patients had further surgery for recurrence of malignancy. Among USCBs, 51.3% of patients (101/196) had one pass, 44.2% (86/196) had two passes, and 4.5% (9/196) had more than three passes.

The range of diagnoses obtained is shown in Table 1. Note that of the 112 FNAC specimens, 53 (47.2%) were adequate, and of the 196 USCB specimen, 103 (52.6%) were considered adequate to obtain a cytological diagnosis. Fifty-seven patients (53.2%) had an initial non-diagnostic FNAC, compared with 13 (4.2%) non-diagnostic USCBs (see Table 2). Of these, eight FNAC and two USCB were repeated and 14 of the FNAC patients proceeded to USCB. Of the 67 patients with an initial non-diagnostic FNAC, malignancy was later confirmed in 25 (37.3%), compared with four (30.8%) of the 13 non-diagnostic USCBs. The remainder of the non-diagnostic samples were confirmed as benign, except for two; one patient had a non-diagnostic FNAC for suspected recurrence of a squamous cell carcinoma and was not further investigated due to disseminated disease, another patient had a non-diagnostic USCB which was not further investigated. Table 3 shows the final diagnosis in patients who had a non-diagnostic biopsy and the method by which this was obtained.

There were 140 patients who underwent USCB, FNAC, or both, but did proceed to definitive surgery. Two patients had non-diagnostic biopsies but were not investigated further. In 132 of the remaining 138 patients (90.6%), the final diagnosis was made by USCB alone. Of the other six patients, three were diagnosed by FNAC alone and three required USCB for non-diagnostic FNAC. Table 4 demonstrates the spectrum of diagnoses in the non-surgical group. The majority were benign (52.3% (72/138) Warthin’s tumour). Of the 11 patients with malignancy, seven were considered inoperable due to disseminated disease and four were unfit for surgery.

**Table 1. Range of diagnoses obtained from the diagnostic ultrasound-guided core needle biopsy (USCB) and fine needle aspiration cytology (FNAC) and surgical excision biopsy (SEB) samples.**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FNAC</th>
<th>USCB</th>
<th>SEB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal tissue</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasmacytoma adenoma</td>
<td>27</td>
<td>112</td>
<td>131</td>
</tr>
<tr>
<td>Warthin’s tumour</td>
<td>13</td>
<td>112</td>
<td>63</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>9</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Bizarre cell adenoma</td>
<td>9</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Morocumulon adenoma</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Oncophyloma adenoma</td>
<td>5</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Myoepithelioma</td>
<td>2</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Microphthlaoma</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Muscle cell adenoma</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Lipoma</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>4</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>5</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Acinar cell carcinoma</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Bizarre cell adenocarcinoma</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated carcinomas</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Keratinizing SCC</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non small cell carcinoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ovarian carcinoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fibroepithelial sarcoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Myoepithelial sarcoma</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Haematological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non Hodgkin lymphoma</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MALT lymphoma</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Plasmocytoma</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>B-cell lymphoma</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Polyclonal lymphoma</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>306</td>
<td>259</td>
</tr>
</tbody>
</table>

**Table 2. Spectrum of pathology findings in non-diagnostic fine needle aspiration cytology (FNAC) and ultrasound-guided core needle biopsy (USCB) results.**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FNAC</th>
<th>USCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflamed mucosa</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>Atypia – suspicious for malignancy but not diagnostic</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>No tumour cells seen but not definitive</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Probable benign neoplasia but not diagnostic</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Equivocal result between benign and malignant pathology</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Haemorrhages</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total non-diagnostic FNAC</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>USCB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflamed mucosa</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Atypia – suspicious for malignancy but not diagnostic</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>No tumour cells seen but not definitive</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Equivocal result between benign and malignant pathology</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total non-diagnostic USCB</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Final diagnosis with initial non-diagnostic fine needle aspiration cytology (FNAC) and ultrasound-guided core needle biopsy (USCB).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FNAC diagnosis</th>
<th>USCB diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical excision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal carcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intraductal papillomatosis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tubular adenoma</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Micropapillary carcinoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Adenomyoepithelioma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Basal cell adenocarcinoma</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Papillary thyroid cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

| Non-surgical excision   |                |                |
| Ductal carcinoma        | 1              | 1              |
| Intraductal papillomatosis | 1            | 1              |
| Tubular adenoma         | 2              | 2              |
| Mucinous cystadenoma    | 3              | 3              |
| Micropapillary carcinoma | 4             | 4              |
| Adenomyoepithelioma     | 1              | 1              |
| Basal cell adenocarcinoma | 2            | 2              |
| Squamous cell carcinoma | 3              | 3              |
| Papillary thyroid cancer | 1              | 1              |
| Malignant melanoma      | 1              | 1              |
| Subtotal                | 8              | 8              |
| Total                   | 10             | 10             |

FNAC: fine needle aspiration cytology; USCB: ultrasound-guided core needle biopsy.

Discussion

Ultrasound imaging is sensitive in identifying parotid lesions and on its own is able to differentiate benign from malignant lesions with an accuracy of greater than 90%. However, due to the overlap in imaging features between benign and malignant lesions, ultrasound in combination with needle biopsy is necessary to improve preoperative diagnosis. The histopathology of salivary gland neoplasia, with overlapping morphological characteristics, often poses a diagnostic challenge for the pathologist.

FNAC is a quick and safe sampling technique that can readily be performed in the outpatient setting. The diagnostic performance of FNAC is enhanced when supervised within a cytological-led service, where the FNA can be assessed immediately and lesions can be re-assessed if required. The use of imaging (ultrasound) guidance and ancillary cytopathological techniques, such as in situ hybridization and flow cytometry, can also improve diagnostic accuracy.

However, these services are expensive and not widely available outside larger and specialist centres, including our centre. This is an important limitation of our study, as we were comparing USCB, performed by a small number of experienced radiologists, with FNAC, performed by various clinicians of varying experience without image guidance or cytology. The rather high non-diagnostic rate of FNAC at our centre (55.8%) compared with reports elsewhere of 14–18%.

As a further point, FNAC performs poorly in the characterization of lymphoid proliferation, as an accurate diagnosis of lymphoma requires architectural assessment of tissue and immunohistochemical staining which is not usually possible on cytology.
Diagnostic investigation of parotid neoplasms

Table 4. Diagnosis obtained by ultrasound-guided core needle biopsy (USCB) and fine needle aspiration cytology (FNAC) in patients where no definitive surgery was performed.

<table>
<thead>
<tr>
<th>Diagnosis Obtained</th>
<th>USCB alone</th>
<th>FNAC and USCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warthin's tumour</td>
<td>68</td>
<td>2</td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>Monomorphic adenoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lipoma</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Myoepithelioma</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Salivary duct adenoma</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>114</td>
<td>7</td>
</tr>
</tbody>
</table>

Malignant neoplasia

<table>
<thead>
<tr>
<th>Diagnosis Obtained</th>
<th>USCB alone</th>
<th>FNAC and USCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Acinar cell carcinoma</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Subtotal</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>

Rheumatological malignancy

<table>
<thead>
<tr>
<th>Diagnosis Obtained</th>
<th>USCB alone</th>
<th>FNAC and USCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular lymphoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Large B-cell lymphoma</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>MALT lymphoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Chronic lymphocytic leukaemia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

FNAC alone

<table>
<thead>
<tr>
<th>Diagnosis Obtained</th>
<th>USCB alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warthin's tumour</td>
<td>2</td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>3</td>
</tr>
</tbody>
</table>

Total: 138

MAL.T, mucosa-associated lymphoid tissue.

The core of tissue provided by USCB, because it is a preoperative rather than an intraoperative biopsy, can be processed for paraffin section histology, which is of higher quality and easier to interpret than frozen section. Furthermore, sections from the core can be used for immunohistochemical analysis, which can help with grading and typing of parotid malignancy, but are crucial in the diagnosis of lymphoma. In our study, 10 of 13 patients with a haematological malignancy were diagnosed conclusively by USCB, only three went on to have surgery for symptom control. In the other three patients, the final diagnosis was made by surgery following equivocal biopsy results; these were all early in the study period. This trend may reflect the increasing acceptance of USCB by haematologists and developing expertise amongst pathologists in the interpretation of USCB.

Following several studies on the performance of USCB have demonstrated the excellent diagnostic yields from USCB of the salivary glands. A meta-analysis looking at the accuracy of USCB in the diagnosis of salivary gland lesions was also compiled recently. Several of the studies included were based on small samples and all the studies included non-neoplastic pathology in their dataset. The degree of heterogeneity observed for the collection of USCB studies was not significant and was much less compared to the FNAC. The diagnostic accuracy of USCB was also significantly higher than FNAC, with a specificity of 100% and a sensitivity of 92%.

We observed relatively high non-diagnostic rates for Warthin's tumour with both FNAC and USCB. Mucoepidermoid carcinoma was mistaken for benign disease by both FNAC and USCB. This may reflect the cystic nature of these tumours, which are therefore more susceptible to giving non-diagnostic results, even if biopsies are guided. The two false-negative results in the USCB group were both well-differentiated parotid malignancies, one of which was revealed to be a well-differentiated basal cell adenocarcinoma and the other a myoepithelial carcinoma on final surgery. Difficulty diagnosing neoplastic lesions is a recognized problem with the cytological sample provided by FNAC, but has not been described previously with USCB. Despite providing a core of tissue, USCB will not usually be able to demonstrate the capsular invasion that occurs with malignant lesions, only

Table 5. Comparison of diagnostic accuracy of ultrasound-guided core needle biopsy (USCB) and fine needle aspiration cytology (FNAC) for the diagnosis of parotid tumours.

<table>
<thead>
<tr>
<th>Feature</th>
<th>FNAC</th>
<th>USCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>True-positives</td>
<td>74</td>
<td>88</td>
</tr>
<tr>
<td>True-negatives</td>
<td>34</td>
<td>32</td>
</tr>
<tr>
<td>False-positives</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>False-negatives</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Number of patients requiring repeat procedures</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Total number of procedures performed</td>
<td>120</td>
<td>113</td>
</tr>
<tr>
<td>Non-diagnostic procedure</td>
<td>67</td>
<td>68</td>
</tr>
<tr>
<td>Diagnostic procedures</td>
<td>53</td>
<td>50</td>
</tr>
<tr>
<td>Number of diagnostic results for which the patient went on to have definitive surgery</td>
<td>48</td>
<td>65</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>79</td>
<td>95</td>
</tr>
<tr>
<td>Specificity</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>85</td>
<td>99</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>64</td>
<td>100</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>92</td>
<td>99</td>
</tr>
<tr>
<td>Non-diagnostic rate</td>
<td>36</td>
<td>4</td>
</tr>
</tbody>
</table>


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being demonstrated in the surgically treated specimen. Triple assessment is important in this setting, as in both cases there was clinical and ultrasound evidence of malignancy.

One main concern regarding parotid biopsy is the risk of tumour seeding. Seeding along needle tracks appears to correlate very finely needle size and is rarely seen in needles less than 1.6 mm. This is thought to be because larger trephine components are aspirated with the cellular elements in larger needles.28 There have been sporadic case of seeding using a 14-gauge Tru-cut needle.29 We did not encounter any cases of tumour seeding with 18- or 20-gauge needles, and previous studies using a similar technique have not reported this complication.29

To our knowledge, this series of USCB and FNAC in the diagnosis of parotid neoplasia is the largest in the literature to date. This study is also the largest series of FNAC and USCB for Warthin’s tumour and pleomorphic adenoma in the literature. Our results for USCB (specificity of 100% and sensitivity of 95%) correlate with those of previous studies. USCB obviated any possible need for surgery in a third (31/398) of the study population. The methods used to perform FNAC and USCB in this study reflect current practice in the Anatomy and Histology District general hospitals and are therefore likely to apply to the real-life situation in most non-specialized units.

USCB at our unit has performed very well and indeed better than optimized FNAC from previous reports.24 USCB provides a highly accurate tool for parotid diagnosis and could be considered as an integral part of triple assessment in patients presenting with a persistent salivary gland mass.

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None.

Competing interests

None.

Ethical approval

Not applicable.

Patient consent

Not required.

References

4.11 Howlett D C, Skelton E, Moody AB

Establishing an Accurate Diagnosis or a Parotid Lump: An Evaluation of the Current Biopsy Methods – Fine Needle Aspiration Cytology, Ultrasound Guided Core Biopsy and Intra-operative Frozen Section.

A.Mandy@brighton.ac.uk

- Subject: David Howlett: PHD by publication

Dear Anne

Re: Howlett DC, Skelton E, Moody AB

Establishing an Accurate Diagnosis of a Parotid Lump: Evaluation of Current Biopsy Methods – Fine Needle Aspiration Cytology, Ultrasound Guided Core Biopsy and Intra-operative Frozen Section.

Accepted for publication, British Journal of Oral and Maxillofacial Surgery, September 2014

I am writing to confirm that David Howlett made a significant contribution to the above paper. David was responsible for paper conception and design, he wrote the provisional manuscript and undertook the literature search. He critically revised the paper with his co-authors and was involved in the final approval of the published version.

With best wishes,

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Establishing an accurate diagnosis of a parotid lump: evaluation of the current biopsy methods – fine needle aspiration cytology, ultrasound-guided core biopsy, and intraoperative frozen section

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Abstract

The optimum technique for histological confirmation of the nature of a parotid mass remains controversial. Fine needle aspiration cytology (FNAC), which has traditionally been used, is associated with high non-diagnostic and false negative rates, and ultrasound (US)-guided core biopsy and frozen section have been explored as alternatives. US-guided core biopsy is more invasive than FNAC, but is safe, well-tolerated, and associated with improved diagnostic performance. Although frozen section offers better specificity than FNAC, it has a number of important drawbacks and cannot be considered as a primary diagnostic tool. US-guided core biopsy should be considered as the initial diagnostic technique of choice, and is used where the accuracy of FNAC is good or when FNAC is equivocal or non-diagnostic.

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Keywords: Fine needle aspiration cytology; Ultrasound-guided core biopsy; Frozen section; Parotid gland lesion

Introduction

To establish an accurate diagnosis of a parotid lump it is now generally accepted that triple assessment, which comprises clinical examination, imaging, and confirmation by biopsy as appropriate, is necessary. Most centres use high-resolution ultrasound as the initial diagnostic imaging of choice as it is quick, safe, and non-invasive, and in experienced hands is capable of a high degree of accuracy. 93% accuracy has been reported for parotid malignancy. For lesions that are large, complex, or likely to be malignant, it guides the need for further investigation, usually with magnetic resonance imaging, but for most focal, and possibly neoplastic lesions, definitive histological confirmation is necessary.

Accurate diagnosis enables the appropriate timing and type of operation (if indicated) and potentially avoids operation in the elderly or unfit, or for certain neoplasms such as Warthin's tumour. It also allows patients to be informed about potential injury to the facial nerve when they give their consent.

Definitive and accurate preoperative diagnosis requires cytological or histological analysis, and the best way to obtain specimens remains controversial. Open surgical parotid biopsy originally fell out of favour because of a number of problems, which included operative complications (injury to the facial nerve and wound infection), delayed complications including formation of a fistula or salivoele, and tumour
recurrence secondary to tumor spillage. Subsequently, by the early 1980s, open biopsy was largely superseded by fine needle aspiration cytology (FNAC), which was traditionally done blind and usually in the outpatient department.

**Fine needle aspiration cytology**

Although successful results have been reported, it has become increasingly clear that there is considerable variability in the accuracy of FNAC, and high nondiagnostic rates and poor sensitivity or specificity have been reported. The technique is well established, and is commonly used as it is quick, safe, relatively non-invasive, and cheap. However, when done blind and by clinicians with different levels of experience, poor technique or inaccurate or insufficient sampling can result in high rates of non-representative or insufficient aspirates.

The perceived and real problems associated with blind FNAC have led clinicians in different specialties to explore ways to improve the diagnostic yield of parotid biopsy procedures. Broadly, they fall into 3 main categories: use of various techniques to improve the yield of FNAC, use of core biopsy with ultrasound (US) guidance, and finally, publication of data that re-examines the use of intraparotid frozen section. Several systematic reviews with meta-analyses on these techniques, and specifically their performance in the parotid glands, have been published, and we will refer to them in the remainder of this article.

Several techniques that can potentially improve the diagnostic yield of FNAC have been described. US-guidance enables precise sampling of the lesion, selectively avoids cystic areas within tumors, and avoids damage to adjacent (vascular) structures. When a cytologist or cytology technician assesses the aspirate at the time of sampling, its performance is further improved. Alternatively, clinical models run purely by a cytologist, which allows repeated sampling of a lesion until a diagnostic aspirate is obtained, have also been described. In larger centres, additional ancillary technology may be available such as in situ hybridisation or flow cytometry to further improve diagnostic rates.

A meta-analysis from 2011, which looked at 84 studies published since the late 1990s, included data on FNAC done both blind and under varying levels of optimised conditions. Overall, it was found to be safe and well-tolerated and had high reported sensitivity (97%) but lower specificity (80%). Diagnoses were found to be reliable, but there was a high false negative rate (20%). Not all the studies included information on non-diagnostic samples, but where available, the rate was found to be around 8%-10%. The analysis also showed a significant wide variation in the performance of FNAC across centres.

**Ultrasonic (US)-guided core biopsy**

US-guided core biopsy was initially established in the diagnosis of breast and abdominal masses, and was first described in the parotid gland in 1990 in a series of 18 patients with parotid lumps. In 13 of them (88%), FNAC had been non-diagnostic, but US-guided core biopsy provided diagnostic specimens in them all. It was found to be better than clinical examination alone in 31% of patients, and in all those operated on, results correlated completely with final histological findings. Subsequently, further meta-analyses of published papers on the efficacy of the technique in the parotid glands have been done.

The technique is well described. It is more invasive than FNAC as it involves local anaesthesia and a small incision in the skin. A needle (usually 18 or 22G) is deployed by means of a spring-loaded automated biopsy device to obtain a core or cores of intact tissue. Crucially, the tissue contains architecturally detailed cells that can be sent for detailed immunohistochemical analysis, which enables confirmation of the type and grade of a tumour and improves the diagnosis of lymphoid hyperplasia. Its ability to diagnose parotid lymphomas is well known, and treatment can now be initiated on the results obtained from core biopsy alone without the need for further investigation.

The ability to provide a core of tissue also means that the technique can be used to make a confident diagnosis of parotid involvement by systemic disease such as lupus.
Sjogren syndrome and sarcoidosis, not usually possible with FNAC.

The most recent summary meta-analysis, which incorporated 12 studies (fewer than those on FNAC) from between 1999 and 2012, reported high overall sensitivity (90%) and specificity (100%), and a non-diagnostic rate of only 1.6%. It supported the safety of the technique in the outpatient department with only 8 complications reported after the procedure (1.6%), and was well-tolerated by patients.

There are concerns about the potential for tumor seeding after US-guided core biopsy. The authors of the meta-analysis acknowledged that the follow-up period for some patients in the studies was low, but no seeding was reported and there have been only sporadic reports after percutaneous needle biopsy. However, continued surveillance is needed as it can occur up to 20 years after the procedure. In a review of seeding after biopsy of salivary gland lesions, only 2 cases were found after large-gauge needle biopsy and 2 after FNAC, noting the larger number of cases and longer follow-up periods for FNAC. The risk of seeding seems to be related to the size of the needle, and is rare with 18/20G needles, which are commonly used in the parotid. Some surgeons excise the tract of the needle core biopsy at the time of operation, although there is no evidence that it is routinely required.

As with FNAC, diagnosis of a well-differentiated malignancy such as basal cell adenocarcinoma with US-guided core biopsy is difficult, as the entire excised specimen must be reviewed and capsular infiltration observed before malignancy is confirmed. Also, as with FNAC, there may be problems with mainly cystic tumours because it can be difficult to obtain enough tissue to make a diagnosis. In this instance, biopsy is essential in all cases. When clinical findings or imaging, or both, suggest malignancy, core biopsy can be repeated or, in a minority of patients, lesions can be excised for formal diagnosis. Frozen section (in situ) could be considered at this stage if clinically appropriate and histological support is available. Intrinsically, however, histological diagnosis is often difficult in these cases, and as the entire lesion is usually required for precise confirmation, formal excision may be preferable.

The use of US guidance can improve the diagnostic accuracy of both core biopsy and FNAC. A study published in 2012 retrospectively compared the accuracy of the 2 techniques in the diagnosis of a parotid mass. Of the 171 patients included, 367 had US-guided FNAC and 64 US-guided core biopsy. Core biopsy had significantly higher sensitivity than FNAC in the differentiation of benign from malignant lesions (94.4% compared with 55.6%), higher specificity (100% compared with 93.3%), and higher accuracy (96.4% compared with 86.9%). In patients with lymphomas, diagnosis was accurate in all 6 who had core biopsy, but in 4 who had FNAC it was not definitive. The authors concluded that US-guided core biopsy was to be preferred over US-guided FNAC "when a definitive diagnosis of a parotid solid mass is needed." Ultrasound uniquely depends on the operator, and sono- graphy examination of the head and neck is recognized as challenging. For US-guided biopsy services to be effective, a pool of trained operators must be available to work across a wide spectrum of institutions. Traditionally, ultrasound has largely been the preserve of radiologists, although this situation is changing, and ultrasound or biopsy examination could be done by interested clinicians with appropriate training and support from radiologists. The Royal College of Radiologists has published useful guidance for training in ultrasound and suggested several levels of experience. We recommend that interested clinicians read these.

Intraoperative frozen section

The meta-analysis of 2011 on intraoperative frozen section looked at 16 studies published between 1985 and 2010. Frozen section in itself has acceptable accuracy (90% sensitivity, 98% specificity) and has been proposed as a confirmatory tool when the results of FNAC are equivocal or non-diagnostic. There are, however, concerns that mirror those associated with open biopsy: risk of tumour spillage and seeding with potential disruption of the operative field for malignant lesions. As previously stated, histological diagnosis of salivary tumours can be complex and challenging, and many histopathologists would be not be comfortable providing a definitive diagnosis using this method. An accurate preoperative diagnosis rather than one obtained intraoperatively brings huge potential benefits to the surgeon and to the patient in terms of informed consent and operative planning.

Conclusion

Preoperatively, one-stop neck lump clinics based on FNAC with support from cytology technicians or cytologists were proposed by the National Institute for Clinical Excellence (NICE)13 but US-guided core biopsy does not lend itself to this type of setting because of the delays involved in the histological reporting of specimens. Improvements in the adequacy and accuracy of the technique compared with FNAC will ultimately facilitate more timely diagnosis and treatment for most patients. Previous work has suggested that alternative mechanisms for the provision of diagnostic clinics can offer equal or more effective care than the models suggested by NICE,14 and it is likely that over time, as in breast practice, US-guided core biopsy will largely replace FNAC in the diagnosis of parotid neoplasms.

Conflict of interest

We have no conflicts of interest.
Ethics statement/confirmation of patient permission

None.

References