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PLENARY ABSTRACT

Imaging in the patient with hyposalivation

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Imaging is not a constant feature of the examination and management of a patient complaining of dry mouth. This review explores the roles for imaging in the patient with a complaint of hypo-salivation.

Does imaging have any value in assessing the presence or the degree of salivary gland involvement in conditions causing hypo-salivation? Does this degree of change correlate to disease severity? Imaging is now used to both assist in the diagnosis of a number of diseases, which result in a sensation of dry mouth, but also to help monitor disease progression and plan intervention.

In diagnosis its role is firstly to differentiate conditions which structurally alter salivary gland tissues from those causing hyposalivation where salivary tissue is grossly unaffected and thus help refine the diagnostic process. Both dehydration and psychogenic causes of hypo-salivation, such as anxiety and depression, would not be expected to alter the gland's structural appearance on imaging. Similarly medication such as antidepressants and antihistamines, give reduced flow but a normal gland appearance. A lack of abnormal findings on imaging should add confidence to these diagnoses, supporting the history and clinical examination, and ruling out other more destructive conditions.

Parenchymal change may be detected on imaging most notably in Sjögren's syndrome (SS). Here the formation of small foci of lymphocytic infiltration throughout the salivary gland parenchyma translates into small sites of multifocal change and gland damage identified throughout the major salivary glands on a variety of imaging modalities, identified in both primary and secondary SS.

The earliest imaging to identify these scattered focal changes was sialography which demonstrates pan-glandular punctate sialectasis as a characteristic feature of SS (Bloch *et al*., 1965, Chisholm *et al.,* 1971). It was postulated that intercalated duct walls are damaged by adjacent developing lymphocytic foci and sialographic contrast media are subsequently forced through the damaged duct walls at multiple and evenly distributed sites throughout the gland parenchyma during the filling phase of sialography to produce the initial radiographic appearance of punctate sialectasis. The interpretation of sialographic change has been shown to be sensitive (as high as 95%) and specific (up to 84%), but is affected by the experience of the observer (Kalk *et al*., 2002).

Sialography remains an objective indicator of salivary gland involvement according to the American-European Classification Criteria for SS (Vitali *et al*., 2002). Authors have plotted the deterioration of the salivary duct architecture from initial presentation as punctate sialectasis through saccular to cavitatory and destructive sialectasis, implying that sialographic imaging may help stage the gland condition in SS (Bloch *et al*., 1965). These ductal changes are, however, a reflection of the effects of obstruction through reduced secretions within the ducts, rather than lymphocytic pathology within the gland parenchyma.

Imaging of gland parenchyma is best achieved on cross-sectional imaging such as computerized tomography (CT) or magnetic resonance imaging (MRI), or ultrasound. CT is described by Harnsberger for detecting microcytic foci and scattered fine calcification within bilaterally enlarging parotid glands, which progresses on to multiple macrocystic and solid nodules (Harnsberger 2004). Interestingly there is little in the literature about CT imaging of SS.

There has been much greater focus on MRI and ultrasound for investigating SS. High sensitivity is reported in the identification of multifocal change in the major salivary glands in SS from both magnetic resonance (MR) and ultrasound imaging. MR imaging and ultrasound both benefit the patient as non-invasive and non-ionising diagnostic tests. MR imaging in the parotid glands reveals multiple low signal foci on T1 imaging and very high signal on T2 weighting, reflecting the watery nature of microcysts. STIR sequences enhance this appearance. MR has been reported as having sensitivity of 81–94% and specificity 93–100% of diagnosing salivary changes associated with SS (Niemela *et al*.,2004; El Miedany *et al.,* 2004). MR sialography is a more recent development; stimulated saliva within ducts and sialectatic spaces gives a bright signal on T2-weighted imaging, and can be rendered from surrounding tissue selectively as a high contrast 2D or 3D 'sialogram'. This has shown high sensitivity (96%) and excellent specificity (100%) in both quantitative and qualitative analysis of characteristic fine multifocal pan-glandular sialectasis (Niemela *et al.,* 2004).

Ultrasound is commonly practiced in Europe and Asia, and is regarded as a more rapid, accessible and less costly option than MR imaging. This technique detects a characteristic sonographic pattern of multifocal reticular parenchymal change throughout the involved superficial portions of the salivary glands in SS, though it is not able, as MR can, to image the full extent of the deep pole of parotid. Nevertheless it has been found valuable in the diagnosis of primary SS by multiple authors, showing a high level of agreement with sialography, scintigraphy, MR imaging and several sets of diagnostic criteria for this disease (El Miedany *et al.,* 2004; Salaffi *et al.,* 2008). Ultrasound and MR appear to offer very similar levels of sensitivity (US 75–90%: MR 94–96%) and specificity (US 84–98%; MR 97–100%) in distinguishing Sjogren's affected glands from normal, and both appear superior to sialography or scintigraphy (Salaffi *et al.,* 2008).

Ultrasound-detectable changes within the glands include an increasing hypoechogenicity, multiple fine hypoechoic foci throughout the salivary glands, bright lines and specked reflections, increased vascularity (seen on colour Doppler ultrasound imaging) and loss of gland definition. Importantly the degree of reticular pattern and change can be correlated to disease progression; a more pronounced honeycomb pattern is noted in more advanced and long-standing disease. Our recent study on a group of 267 patients with a complaint of xerostomia examined on an Oral Medicine clinic has looked at the degree of salivary gland involvement seen on high-resolution ultrasound and scored this using features such as echogenicity, degree of honeycomb pattern, extent of gland involvement and the presence of particularly enlarged hypoechoic foci. This quantification was compared with a diagnosis of SS made strictly on the American-European Classification criteria (Vitali *et al*., 2002) and found the more severe ultrasound changes to be associated with primary rather than secondary SS, and with those who were ENA positive and ANA positive rather than those who were seronegative (Brown 2009). Sensitivity using this scoring system, in bilaterally involved glands of patients with xerostomia, was 97% and specificity 92%. The negative predictive value was 98% and is likely to be particularly useful as it would enable the radiologist to exclude SS with a high degree of confidence when ultrasound reveals normal glands.

A particular feature of the group studied above was the formation, in some individuals, of more marked and larger hypoechoic intraglandular foci. These foci have occasionally been reported (Lewis *et al.,* 2007) and in our group were mostly cystic but, in some cases, developed strong and sometimes disorganized internal vascularity on colour Doppler sonography suggesting a solid and more sinister pathology. Biopsy revealed progression to Mucosal-Associated Lymphoid Tissue (MALT) lymphoma; the 3rd most common of the non-Hodgkin lymphoma group and the commonest lymphoma to affect the salivary glands, with an 18x increased incidence in SS. Ultrasound may therefore play a very useful role in non-invasive monitoring of the salivary glands for MALT lymphoma change in those with long-standing SS.

Other diseases associated with reduced salivary production and which cause structural change within gland parenchyma that may be detected on imaging include; salivary gland agenesis, radiation-induced sialadenitis, sarcoidosis, HIV, diabetes mellitus and cirrhosis. Of these, sialadenitis, sarcoidosis and HIV associated salivary gland disease, as diffuse infiltrative lymphocytic syndrome (DILS), give multi-focal parenchymal change and are most like Sjögren's syndrome on imaging. These conditions in particular require clear differentiation on clinical grounds.

Diffuse inflammatory salivary gland conditions cause changes which are often apparent following localized head and neck radiotherapy and acute sialadenitis – the former causing extended or permanent dry mouth and the latter transient xerostomia. Here all affected salivary gland tissue can assume a heterogeneous appearance on both ultrasound and other cross-sectional imaging techniques and may include multiple small sialocoeles; again clinical correlation is essential.

In assessing salivary gland involvement and surveying for deterioration imaging may show both structural and functional aspects of the salivary glands' status. Radioisotope imaging, in the form of salivary scintigraphy, quantifies salivary gland function and thus represents an alternative to the anatomical depictions of the imaging described above. This would be expected to show a reduction in those conditions, such as SS, which undergo a quantitative reduction in salivary production but is not regarded as a highly specific indicator of any single hyposalivatory condition (Salaffi et al., 2008).

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