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Review Article

Diffusion-weighted magnetic resonance imaging: its uses in otolaryngology

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Abstract

Over recent years, there has been an increase in otolaryngology publications concerning diffusion-weighted magnetic resonance imaging. The aims of this review paper are to summarise the basic principles of diffusion-weighted magnetic resonance imaging, and to provide an overview of current otolaryngological applications and areas of research. Diffusion-weighted magnetic resonance imaging is a radiological technique which has shown promising results in various areas of otolaryngology. However, studies of diffusion-weighted magnetic resonance imaging are difficult to compare, as different imaging parameters and techniques have been used. The role of this imaging modality within otolaryngology is yet to be fully elucidated. Diffusion-weighted magnetic resonance imaging may prove to be a useful adjunct in both the pre- and post-operative care of otolaryngology patients.

Key words: Diffusion Magnetic Resonance Imaging; Echo-Planar Imaging; Head And Neck; Otolaryngology

Introduction

The aims of this review are to summarise the basic principles of diffusion-weighted magnetic resonance imaging (MRI), and to provide an overview of current otolaryngological applications and areas of research.

The Cochrane ENT group trials register, Dare, the Cochrane central register of controlled trials, Medline (1950–2008), Pub Med and Embase (1960–2008) were searched in February 2008 using the following keywords: 'diffusion', 'magnetic resonance imaging' and 'diffusion magnetic resonance imaging'. Any papers referring to diffusion-weighted MRI and applications within otolaryngology were identified and reviewed. The reference lists of selected studies were scanned for additional research material.

History of diffusion-weighted magnetic resonance imaging

Diffusion-weighted MRI has become popular in recent years, with an increase in the number of reports within the radiology literature. The concept of diffusion-weighted MRI is not new. The technique was described in the 1950s, when it was utilised in neurophysiology and in the investigation of acute cerebral ischaemia. It can demonstrate cerebral infarction within minutes of clinical onset, and is used in many centres to diagnose cerebrovascular events.[1] With recent advances and the availability of more powerful MRI machines and image acquisition sequencing techniques, newer areas of research have been identified regarding potential applications of diffusion-weighted MRI. Apart from its use in neurophysiology and otolaryngology, it is also used in the investigation of liver, renal, pancreatic and prostate disease.[2]

Diffusion-weighted magnetic resonance imaging: what is it?

Regular MRI techniques use a homogeneous magnetic field to excite water molecules. When the magnetic field is applied, the protons within the water molecules align along the magnetic field and also begin to spin (i.e. 'precess'). The amount of precession is directly proportional to the strength of the magnetic field and the length of time it is applied. Measurement of the proton precession can be used to produce a T1-weighted image.

When the magnetic field is stopped, the stimulus for proton precession is removed. The speed with which each proton stops spinning (i.e. 'relaxation') differs slightly depending upon the local environment of each individual proton. Measurement

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of this relaxation phase gives rise to a T2-weighted image.

Diffusion-weighted MRI differs from regular MRI in that it uses pulsed (i.e. non-homogeneous) magnetic fields of varying strength, direction and time intervals to excite the protons in water molecules.

In nature, water molecules are in a constant state of motion (termed Brownian motion). Diffusion-weighted MRI essentially measures the Brownian motion of water molecules. The initial position of the water molecules is measured using a pulsed magnetic field. After a time interval (50 milliseconds is typically used in clinical diffusion studies), a second magnetic field gradient pulse is applied to measure the new position of the water molecules (this second magnetic field is of the same time duration and direction as the initial magnetic field pulse but of opposite magnitude). During this time interval (between application of these 'paired' magnetic fields), some water molecules will have reverted to their original starting position (thus, these appear relatively stationary), whereas other water molecules will be in a new position compared with their initial starting point (these have 'diffused'). 'Stationary' water molecules would not be affected by the pair of magnetic field pulse gradients and would retain their MR signal, whereas diffused water molecules that are no longer in their starting position will show a loss of MR signal. The movement of these water molecules can be used to calculate the 'water diffusion coefficient'.

However, in some tissues the diffusion of water is not equal in all directions – the movement of water molecules will also be influenced by the microstructural architecture and the pathophysiological state of the tissue they are in. For example, in white matter water molecule movement parallel to the axon direction will be greater than water molecule movement perpendicular to the axon direction. In the prostate gland, water diffusion is greater along the direction of the prostatic ducts. Furthermore, damaged tissue will have increased permeability of its cell membranes, and therefore water molecule movement will be greater than in normal, healthy tissue.

To acknowledge this, the water diffusion coefficient in tissues is termed 'apparent diffusion coefficient'. The apparent diffusion coefficient is typically calculated by measuring the movement of water molecules in three directions which are all perpendicular to each other (i.e. an *x* axis, *y* axis and *z* axis). The movement of the water molecules can be measured in more than three directions; this is termed 'diffusion tensor imaging' when at least six directions are used.

The magnitude and direction of the applied magnetic field gradients and the time between the paired gradients is determined by the type of diffusion MR sequencing technique used and by an image acquisition parameter called the b-value (measured in seconds/mm^2).

Examples of different types of MR diffusion sequencing techniques include echo planar imaging and non-echo planar imaging (e.g. fast asymmetric spin echo, single shot spin echo and multi-shot spin echo). Each type of image sequencing has unique properties such as spatial resolution, motion artefact and chemical artefacts. The larger the b-value, the greater the time between the paired magnetic field gradients and therefore the greater the sensitivity to slower water molecule movement and smaller diffusion distances. A b-value of 0 seconds/mm^2 is analogous to a T2-weighted image. Typical settings used to image the brain use b-values between 0 and 1000 seconds/mm^2.

With this multitude of technical variations and terminology, it is unsurprising that diffusion-weighted MRI can cause confusion amongst non-radiologically trained clinicians. To allay such confusion, the following section details possible applications of diffusion-weighted MRI within the field of otolaryngology.

Applications in otolaryngology

Middle-ear cholesteatoma

Early studies have used diffusion-weighted MRI echo planar imaging to identify cholesteatoma. However, this form of imaging is prone to interface artefact (bone and air) and image distortion, and has a low spatial resolution. It can only detect cholesteatomas sized 5 mm or larger.[3–5] A different sequencing technique, non-echo planar imaging, has the advantage of higher spatial resolution and less susceptibility artefacts, and has been reported to demonstrate cholesteatomas as small as 2 mm in non-operated patients.[6] To date, studies using diffusion-weighted MRI to detect residual or recurrent cholesteatoma have reported a range of accuracies. This range of results could be explained by the relatively small number of patients, the time interval between patients undergoing their diffusion-weighted MRI scan and the actual date of their operation (where the scan result can be confirmed or refuted) and the different types of diffusion-weighted MRI sequencing techniques used (Table I).

Some centres use a combination of computed tomography (CT) and MRI, including diffusion-weighted techniques (echo planar imaging and non-echo planar imaging), in the pre-operative evaluation of patients with cholesteatoma, and also follow up their patients at one and five years with diffusion-weighted MRI to identify those who require a 'second look' CT scan. In one centre, this approach dramatically reduced the rate of second look operations, from 62 per cent to less than 10 per cent.[10] This has financial benefits, as a reduction in surgical procedures far outweighs the cost of multiple scans. There is also the added benefit of reducing the potential surgical morbidity.

Petrous bone cholesteatoma

Fitzek *et al.* compared echo planar diffusion-weighted MRI for 15 patients with petrous bone cholesteatoma, 12 patients with acute otitis media and 20 healthy volunteers.[11] They found that diffusion-weighted MRI correctly identified 13 of 15 patients with

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TABLE I

STUDIES OF CHOLESTEATOMA AND DIFFUSION-WEIGHTED MRI: SUMMARY

Study	Pts (*n*)	DW-MRI type (b-value)	Time		Sens (%)	Spec (%)	PPV (%)	NPV (%)	Cholesteatoma size missed (mm)
			1st surg to DW-MRI scan	DW-MRI scan to subsequent surg					
Aikele *et al.*[5]*	22 (only 17 had surg)	EPI (1000)	Mean 6 yr 9 mth (range 4 mth to 31 yr)	≤11 mth	77	100	100	75	<5
Stasolla *et al.*[4]	18	EPI (500 & 1000)	7–19 mth	≤15 days	86	100	100	92	2
Stasolla[7†]	24 (only 19 had prev cholesteatoma surg)	EPI (50, 500 & 1000)	9–18 mth	≤15 days	92	100	100	92	2
Vercruysse *et al.*[3‡]	100 (only 45 had prev cholesteatoma surg)	EPI (0 & 1000)	8–18 mth	Mean 15 days (range 1–57 days)	12.5	100	100	72	<4
Dubruelle[8**]	24	Non-EPI (800)	N/A	≤5 mth	100	91	93	100	None missed
Jeunen[9]	31	EPI (500 & 1000)	N/A	Mean 2.9 mth (range 0.5–16 mth)	54	90	92.3	47.4	<5
De Foer *et al.*[6]	32 (only 19 had surg)	Non-EPI (0 & 1000)	10–18 mth	N/A	90	100	100	96	2

*Sens, spec, PPV and NPV are given for using a combination of DW-MRI and traditional MRI. †Five patients had suspected primary acquired cholesteatoma. ‡Remaining 55 patients had suspected primary acquired cholesteatoma; in this group, DW-MRI sens, spec, PPV and NPV were 81, 100, 100 and 40%, respectively, and the size of cholesteatoma missed was 5–21 mm. **All patients had either a previous canal wall up or canal wall down operation. Pts = patients; DW-MRI = diffusion-weighted magnetic resonance imaging; surg = surgery; sens = sensitivity; spec = specificity; PPV = positive predictive value; NPV = negative predictive value; EPI = echo planar imaging; yr = years; mth = months; prev = previous; N/A = information not available

petrous apex cholesteatoma (sensitivity 87 per cent). Of the two patients who were missed, one had an epitympanic retraction pocket with no discernable keratin accumulation, and in the second patient the cholesteatoma mass (size unreported) had spontaneously extruded into the external auditory canal. Two of the patients with acute otitis media had a high signal intensity on diffusion-weighted MRI; the remaining 10 patients, and all 20 healthy volunteers, had low intensity signals on diffusion-weighted MRI scans (specificity 94 per cent).

Facial nerve imaging in vestibular schwannoma

Toaka *et al.* performed diffusion tensor MRI scanning in eight patients to visualise the facial nerve prior to vestibular schwannoma removal; the tract of the facial nerve at the time of surgery was compared to the predicted facial nerve tract from preoperative diffusion-weighted MRI scanning.[12] The authors identified the facial nerve between the brainstem and internal acoustic meatus using the scan in seven of the eight cases. The predicted facial nerve course agreed with the surgical findings in five of seven cases (in the remaining case, intra-operative visualisation of the facial nerve was not possible due to the large tumour size).

Head and neck cancer

In cases of head and neck cancer, the primary site disease is usually well defined by conventional MRI and CT scans. However, there can be uncertainty in determining the presence of non-palpable metastatic lymph nodes in the neck, and in differentiating between post-treatment tissue changes and recurrent or residual disease. In these cases, diffusion-weighted MRI amy play a role.

Staging neck lymph nodes in squamous cell carcinoma

Abdel Razek *et al.* assessed 31 patients with neck lymphadenopathy and suspected malignancy (either primary origin or secondary nodal disease).[13] All patients underwent echo planar diffusion MRI. The apparent diffusion coefficient was calculated for the suspected lymph nodes and correlated with histological findings (14 neck dissections, nine surgical biopsies and eight core biopsies). Eighty-seven enlarged lymph nodes were found in the 31 patients. Histological analysis revealed metastatic head and neck carcinoma (51 nodes), lymphoma (21) and benign lymphadenopathy (15). Diffusion-weighted MRI was found to have a sensitivity and specificity of 98 and 88 per cent, respectively, in differentiating between malignant and benign lymph nodes.

Sumi *et al.* used echo planar diffusion MRI to calculate the apparent diffusion coefficient of 55 lymph nodes prior to surgical removal.[14] Histological analysis revealed 25 metastatic lymph nodes, 25 nodes with benign lymphadenopathy and five lymphomas. The apparent diffusion coefficient was significantly greater for metastatic lymph nodes than for benign lymphadenopathy. Furthermore,

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the apparent diffusion coefficients for highly or moderately differentiated cancers were significantly greater than those for poorly differentiated cancers.

Differentiating post-treatment tissue changes from tumour recurrence

Studies to date have shown promising results for the use of diffusion-weighted MRI in this area. Abdel Razek *et al.* investigated 32 patients clinically suspected of recurrent head and neck cancer following treatment (surgery and/or radiotherapy).[15] These patients' primary cancers included a variety of sites and histopathologies. Diffusion-weighted MRI was used to calculate the apparent diffusion coefficient of the suspected recurrent or residual disease tissue, and this value was correlated with pathological results. Abdel Razek *et al.* found a statistically significant difference in apparent diffusion coefficient values, comparing patients with recurrent or residual disease with those found to have post-treatment tissue changes only. The sensitivity and specificity of diffusion-weighted MRI were quoted as 84 and 90 per cent, respectively, for differentiating between recurrent or residual disease and post-treatment tissue changes.

Vandecaveye *et al.* studied 26 patients with suspected persistent or recurrent squamous cell carcinoma in the head and neck (18 had suspected disease in the primary tumour site and eight had suspected disease in neck lymphadenopathy).[16] All patients had CT and echo planar diffusion MRI scans; 17 patients also had positron emission tomography (PET) scans prior to salvage surgery (this included laryngectomy, hemiglossectomy, and unilateral or bilateral neck dissection). Primary treatment comprised (chemo)radiotherapy either with or without surgery. Apparent diffusion coefficients were calculated for the suspected tumour site and for the surrounding, irradiated, disease-free tissue. Imaging results were correlated with histopathological results. The apparent diffusion coefficient values were significantly less for tumour tissue than for non-tumour tissue, with a sensitivity and specificity of 94.6 and 95.9 per cent, respectively. Diffusion-weighted MRI also yielded fewer false positives than PET, and detected involved nodes less than 1 cm in size. There were two false negatives: two patients with micro-metastases (<3 mm) in lymph nodes which had not been detected by either diffusion-weighted MRI or PET.

Head and neck abscess

Kito *et al.* investigated whether diffusion-weighted MRI could accurately detect abscess formation in the head and neck.[17] Their patient sample size was small – they compared 10 healthy volunteers with 10 patients with a head or neck abscess collection. The abscesses were predominately in the submandibular, buccal and masticator spaces, and were dental in origin. The apparent diffusion coefficient values were calculated and correlated with the surgical findings. Diffusion-weighted MRI was found to accurately identify abscess formation in only 50 per cent of cases.

Salivary glands

Diffusion-weighted MRI has also been used in the functional evaluation of salivary glands. Studies have shown a small correlation between decreased salivary function (measured by scintigraphy) and apparent diffusion coefficient values.[18–20] Another study has used diffusion-weighted MRI to try to differentiate between benign and malignant salivary gland tumours.[21] In this latter study, the histological results for 45 parotid glands were correlated with the apparent diffusion coefficient values obtained pre-operatively. The apparent diffusion coefficient values did differentiate between benign and malignant tumours, but differentiation between the various histological types of cancer was not possible. However, apparent diffusion coefficient values for salivary glands in normal, healthy volunteers have shown considerable heterogeneity.[22,23] Therefore, further studies are required to investigate the role of diffusion-weighted MRI in salivary gland disease.

Conclusion

Diffusion-weighted MRI is an imaging technique which has shown promising results in various areas of otolaryngology. It is a non-invasive technique which can be performed on modern MRI scanners used to obtain traditional T1- and T2-weighted MR images.

However, there is limited knowledge of this imaging technique amongst otolaryngologists and radiologists. As the studies above show, there are many different diffusion-weighted MRI sequencing techniques, all of which differ in terms of b-values and other parameters such as coil positioning and strength. A standardised technique would be desirable to assist the introduction of diffusion-weighted MRI to more centres, and to facilitate the generation of further studies. In addition, the interpretation of diffusion-weighted MR images can be challenging, and requires appropriate training and experience for the otolaryngologist and radiologist.

The role of diffusion-weighted MRI within otolaryngology is yet to be fully elucidated. This imaging technique may prove a useful adjunct in both pre- and post-operative care of otolaryngology patients.

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