The role of magnetic resonance imaging in the identification of suspected acoustic neuroma:
a systematic review of clinical and cost-effectiveness and natural history

CRD summary
This review concluded that the generally poor evidence indicated that magnetic resonance imaging should be the first-line investigation for the identification of acoustic neuroma (benign cranial nerve tumours) in appropriately selected patients. Although the authors’ conclusions appeared to reflect the evidence available, given limitations with the included studies and the reporting in the review, they should be interpreted with caution.

Authors' objectives
To assess the clinical and cost-effectiveness of various diagnostic tools in the identification of acoustic neuroma in patients with unilateral hearing loss and/or tinnitus.

Searching
Sixteen databases were searched between 1980 and October 2006, including EMBASE, MEDLINE, BIOSIS Previews, Cochrane Central Register of Controlled Trials (CENTRAL), DARE and CINAHL. An updated search of MEDLINE, EMBASE, PubMed and HEED was undertaken from October 2006 to August 2008. Search terms were reported. In addition, appropriate databases and research registers were searched in an attempt to locate grey (unpublished) literature.

Study selection
Studies comparing an investigative test with magnetic resonance imaging (MRI, reference test) in patients, over the age of 16 (or studies with only a small number of patients under the age of 16), with unilateral sensorineural hearing impairment, asymmetric sensorineural hearing impairment, or unilateral tinnitus, were eligible for inclusion. Eligible studies were required to report sensitivity/specificity of the diagnostic test, or present data from which these could be calculated. Studies published before 1990 were excluded, as were studies in which patients with neurofibromatosis type 2 could not be excluded.

The majority of included studies were conducted in the USA. Where reported, ages ranged between 13 and 87. Tumour sizes varied considerably. Studies either compared the use of auditory brain-stem response with MRI, or compared high-resolution imaging without gadolinium (T2W or T2*W properties) versus gadolinium-enhanced imaging (gold standard GdT1W sequence). Some studies comparing auditory brain-stem response with MRI also reported the use of radiology, surgery or computerised tomography (CT)/MRI as comparators. Auditory brain-stem response criteria for hearing abnormality varied between studies. Some individual studies reported other outcomes, including positive predictive value (PPV), negative predictive values (NPV) inter-aural difference of wave V latencies, and inter-peak latency.

The authors stated that clinical and methodological experts selected papers for review, but no further details were provided.

Assessment of study quality
Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool.

The authors did not state how may reviewers performed the validity assessment.

Data extraction
The number of patients/ears identified, with or without acoustic neuroma, with MRI or other investigative tests (i.e. true positives, true negatives, false positives and false negatives), and sensitivities and specificities, were extracted into a 2x2 table. Where sensitivity and specificity were not reported, these were calculated from the data available, along with their 95% confidence intervals (CIs).
The authors did not state how many reviewers extracted the data.

Methods of synthesis
A random-effects model was used to pool sensitivities and specificities according to the comparative investigative test (i.e. auditory brain-stem response or alternative MRI). Statistical heterogeneity was assessed using the $X^2$ and $I^2$ statistics. Sensitivity analyses were conducted according to the categories of acoustic neuroma size (up to 1.0 cm, 1.0 to 2.0cms, and above 2.0cms) in studies comparing auditory brain-stem response versus MRI.

Results of the review
Twenty seven studies were included in the review. Sample sizes ranged from 20 to 1,233 participants. Most of the studies were retrospective. One study comparing auditory brain-stem response with magnetic resonance imaging (MRI) comparison, and three studies comparing MRI were not included in the pooled synthesis; the reasons for this were unclear. The quality of studies using auditory brain-stem response as the comparator ranged between 5 and 11, with only one study scoring greater than 10. Studies comparing MRI reported quality scores ranging between 9 and 13, with most scoring more than 10.

Auditory brain-stem response versus MRI (16 studies, n=2,649 patients): Auditory brain-stem response showed high sensitivity (identified a higher rate of true positives) compared with MRI, with a pooled sensitivity of 0.85 (95% CI 0.82 to 0.87; 15 studies). Sensitivity analyses indicated that sensitivity was dependent on the size of the tumour, with high levels of sensitivity using auditory brain-stem response reported in patients with tumours larger than 1cm and not in patients with smaller tumours. Only three studies reported specificity, which was also high for auditory brain-stem response compared with MRI (identified a higher rate of true negatives), with a pooled specificity of 0.77 (95% CI: 0.73 to 0.81).

There was significant statistical heterogeneity among studies reporting sensitivity (p<0.0001; $I^2$=88%) and specificity (p<0.001; $I^2$=86%). Sensitivity analyses significantly reduced statistical heterogeneity, which was no longer significant for each category of tumour size.

High-resolution imaging without gadolinium versus gadolinium-enhanced imaging (11 studies, n=2,572 patients): High-resolution imaging without gadolinium (T2W or T2*W properties) had high sensitivity (good test accuracy) compared with the gold standard gadolinium-enhanced imaging (GdT1W sequence) MRI: T2W sensitivity was 98% (95% CI 94 to 99; five studies); T2*W sensitivity was 96% (95% CI 86 to 99; three studies - 98%, 95% CI 95 to 99% according to forest plot). The pooled specificity for T2W was 96% (95% CI 94 to 96; five studies) and for T2*W 97% (95% CI 95 to 98; three studies). There was evidence of statistical heterogeneity among studies reporting specificity (T2W $I^2$=87.8% and T2*W $I^2$=92.8%).

Cost information
A separate systematic review was undertaken in the section to evaluate cost-effectiveness.

Authors' conclusions
The majority of the available evidence was poorly reported, but indicated that auditory brain-stem response can no longer be considered the primary test to screen for acoustic neuroma. Rather, magnetic resonance imaging (MRI) should be the first-line investigation in appropriately selected patients. Where non-contrast high-resolution three-dimensional T2W or T2*W sequences provide diagnostic confidence, inclusion of gadolinium (GdT1W) sequences are unlikely to contribute any further relevant information.

CRD commentary
The review question and inclusion criteria were clearly defined. An extensive search of the literature was undertaken, including attempts to locate grey (unpublished) literature, reducing the possibility that potentially relevant papers were missed. The quality of the studies was assessed and indicated varying levels of quality for different comparisons. The authors did not report how the quality assessment was performed or how data were extracted, and only briefly outlined how studies were selected. Therefore, reviewer error and bias may have been introduced.
Appropriate methods were used to pool the data and assess for statistical heterogeneity, which was evident for most comparisons. Details on tumour size were reported, but as other patient details were not reported, it was unclear whether the patients were comparable at baseline. The authors acknowledged certain limitations with the individual studies, such as poor reporting and the potential for selection bias.

Although the authors' conclusions appeared to reflect the evidence available, given the above limitations, their conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors stated a number of issues that need to be taken into consideration when determining the most appropriate approaches to imaging, including the standardisation and specification of the measurement tools used to document acoustic neuroma size, to minimise inter- and intra-observer variation at follow-up.

Research: The authors stated that there is a need for collaborative and multi-centre studies to ensure that findings are timely, apply to current practice and have sufficient sample sizes to draw robust conclusions. A systematic review was also recommended to address the issues of treatment strategies and outcomes to enable useful knowledge gathering and dissemination.

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