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FULL PAPER

Should we be moving to a national standardized non-gadolinium MR imaging protocol for the surveillance of vestibular schwannomas?

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Objectives: To examine whether the model of Getting It Right First Time (GIRFT) could be relevant to the surveillance of non-operated vestibular schwannomas (vs) by testing the following hypotheses: (1) in the UK there is a great variation in the imaging protocol for the follow-up of vs; (2) high-resolution, T_2 weighted MRI (HRT₂W-MRI) has an equivalent accuracy to gadolinium-enhanced T_1 weighted MRI (Gd-MRI) in the assessment of vs size and; (3) imaging with HRT₂W-MRI rather than Gd-MRI could offer financial savings.

Methods: Two neuroradiologists independently performed measurements of 50 vs imaged with HRT₂W-MRI and Gd-MRI. Differences in mean tumour measurements between HRT₂W-MRI and Gd-MRI were determined, as were intra- and interobserver concordance. Level of agreement was measured using Bland-Altman plots. Consultant neuroradiologists within 30 adult neurosurgical units in the UK were contacted via email and asked to provide the MRI protocol used for the surveillance of non-operated vs in their institution. The financial difference between scanning with HRT₂W-MRI and Gd-MRI was determined within Leeds Teaching Hospitals NHS Trust.

Results: There was no statistically significant difference in the mean diameter of vs size, measured on HRT₂W-MRI and Gd-MRI ($p = 0.28$ & $p = 0.74$ for observers 1 and 2 respectively). Inter- and intraobserver concordance were excellent (Interclass correlation coefficient = 0.99, Interclass correlation coefficient ≥ 0.98 respectively). Differences between the two sequences were within limits of agreement. 26 of 30 UK neuroscience centres (87 % response rate) provided imaging protocols. 16 of the 26 (62%) centres use Gd-MRI for the surveillance of vs. HRT₂W-MRI is £36.91 cheaper per patient than Gd-MRI.

Conclusion: Variation exists across UK centres in the imaging surveillance of non-operated vs. HRT₂W-MRI and Gd-MRI have equivalent accuracy when measuring vs. Imaging with HRT₂W-MRI rather than Gd-MRI offers potential financial savings.

Advances in knowledge: This study highlights the potential health and economic benefits of a national standardized imaging protocol for the surveillance of non-operated vs.

INTRODUCTION

Getting It Right First Time (GIRFT) is a UK national programme designed to improve the quality of care within the NHS by reducing unwarranted variations. By tackling variations in the way services are delivered across the NHS, and by sharing best practice between trusts, GIRFT identifies changes that will help improve care and patient outcomes, as well as delivering efficiencies such as the reduction of unnecessary procedures and cost savings.¹ Imaging performed for the surveillance of patients with

non-operated brain tumours such as vestibular schwannomas is a practice that may benefit from the GIRFT model.

Vestibular schwannomas (vs), also known as acoustic neuromas, are benign tumours that originate from the Schwann cells of the vestibular nerve sheath and typically occur in the cerebellopontine angle and internal auditory canal.² They account for 10% of all brain neoplasms and studies have approximated their incidence to 10–20 cases per million people per year, although this is likely an

underestimate.^{3–5} 30 to 90% of *vs* grow and those that do, typically grow slowly, less than 2 mm/year.^{6,7}

Presently, gadolinium-enhanced T_1 weighted imaging (Gd-MRI) is considered the gold-standard for detecting *vs*.^{7,8} Irrespective of the management stratification (surgery versus stereotactic radiosurgery versus conservative) patients with *vs* typically undergo multiple episodes of Gd-MRI under a protocol of serial surveillance imaging in which measurements of the *vs* are obtained to gain information on tumour growth. For example, in Leeds Teaching Hospitals NHS Trust our institution patients known to have *vs* currently undergo surveillance imaging at 1, 2, 3, 5, 7 and 10 years following initial diagnosis. If an extrameatal tumour has a maximal intracranial dimension of 20 mm or more at initial presentation, an early 6 month interval MR scan may be considered. The basis for an additional 6 month scan in extrameatal tumours is to ensure that rapidly growing tumours are picked up at the earliest opportunity. Close observation is recommended during the first 3 years as 90% of growing tumours are detected within the first 3 years of surveillance.⁹ At the completion of surveillance, if the patient is aged 45 years or under, consideration is given to further surveillance imaging at 5 year intervals for a maximum of 15 years. This regime is applied in cases of *vs* measurement stability with the intervals shortening should any growth be shown. This same protocol of imaging at 1, 2, 3, 5, 7 and 10 years post-irradiation treatment is applied for patients following γ knife therapy.

As an alternative to Gd-MRI some studies advocate the surveillance of *vs* with high-resolution T_2 weighted MRI (HRT₂W-MRI) typically utilizing steady-state sequences that provide high spatial resolution without the use of intravenous contrast agents (e.g. CISS (Siemens, Erlangen, Germany), SPACE (Siemens, Erlangen, Germany), DRIVE (Driven Equilibrium Radiofrequency Reset Pulse, Philips Medical Systems, Best, Netherlands) or FIESTA-C (Fast Imaging Employing Steady-state Acquisition Cycled Phases, GE, General Electric, Milwaukee, WI)).¹⁰ The use of HRT₂W-MRI in the detection of *vs* is not new, having been described as an useful imaging technique since the early 1990's but its prevalence as a surveillance technique is currently unknown.

To examine whether the imaging protocol performed for the surveillance of patients with non-operated *vs* is a practice that may benefit from the GIRFT model, we hypothesised the following: (1) in the UK there is great variation in the imaging protocol for the follow-up of *vs*; (2) imaging with HRT₂W-MRI rather than Gd-MRI could offer financial savings and; (3) HRT₂W-MRI has an equivalent accuracy to Gd-MRI in the assessment of *vs* size.

METHODS AND MATERIALS

This study was reviewed and approved by the local research and development department. Formal ethics approval was waived as the project was deemed to fall under the category of "service evaluation".

Patient selection

MRI was acquired prospectively from 1 November 2017 in 50 consecutive patients undergoing surveillance of non-operated *vs*. Patients who had undergone prior operation for a *vs*, those treated with stereotactic radiotherapy and those patients with neurofibromatosis Type II were excluded (Gd-MRI is generally required in post-operative scans to differentiate residual tumour from post-operative phenomena and can be useful in patients with neurofibromatosis to allow detection of additional nerve sheath tumours and meningiomata).

MR imaging

All examinations were performed on either an Avanto or Aera (Siemens Healthineers, Erlangen, Germany) 1.5 T system using standard head coils. The MRI protocol included: axial T_2 weighted turbo spin echo images [repetition time/echo time (TR/TE), 5420/96 ms; field of view (FOV) 230 × 200 mm, slice thickness, 5 mm; interslice gap, 0.5 mm; matrix, 293 × 448; and NEX, 1], axial T_1 pre- and post-gadolinium and coronal T_1 post-gadolinium spin echo images (TR/TE, 490/15 ms; FOV 200 × 180 mm, slice thickness, 3 mm; interslice gap, 0.3 mm; matrix, 216 × 320; and NEX, 2), and either (1) 3D CISS (Constructive Interference in Steady State) images (TR/TE, 11.56/5.78 ms; FOV 200 × 180 mm, slice thickness, 0.7 mm; matrix, 192 × 256; and NEX, 1) or (2) 3D SPACE (Sampling Perfection with Application optimized Contrast by using different flip angle Evolutions) images (TR/TE, 1200/267 ms; FOV 200 × 200 mm, slice thickness, 0.6 mm; matrix, 216 × 320; and NEX, 1.6). For contrast-enhanced sequences patients received a single 10 ml bolus of gadolinium (DOTAREM®, gadoterate meglumine, Guerbet, Netherlands) if they weighed ≥50 kg. If <50 kg, patients received 0.2 ml kg⁻¹.

Image analysis

Two experienced consultant neuroradiologists (Observer 1 with 3 years of neuroradiology reporting; Observer 2 with 12 years) independently performed measurements on either HRT₂W-MRI or Gd-MRI examinations without reference to the other sequence. Each observer was blind to all previous measurements and to the clinical reports. The clinical stages of the *vs* were determined according to the Koos classification, which is as follows: Grade I intracanalicular tumour; Grade II small tumour protruding at the cerebellopontine angle, up to 2 cm; Grade III tumour which occupies the cerebellopontine angle cistern, with no displacement of the cerebral trunk, up to 3 cm; and Grade IV large tumour, with displacement of the trunk or cranial nerves, >3 cm.¹¹ Vestibular schwannomas were measured on axial images using the institutional picture archiving and communication system (PACS, Impax v. 6.5.3.3009, Agfa Healthcare, Mortsel, Belgium) with electronic callipers on a submillimeter (mm) scale. A single maximal transverse diameter was recorded for those tumours confined to the internal auditory canal. For those tumours that extended into the cerebellopontine angle cistern, a single maximal cisternal diameter was also recorded (Figure 1). This replicated the same technique and measurements used in routine clinical practice.

The cases were anonymized and randomly allocated by one of the researchers to Observer 1 and 2. There was a minimum

Figure 1. Example of a single maximal transverse diameter measurement of a left-sided intracanalicular vestibular schwannoma on a single patient using (A) axial HRT₂W-MRI (CISS imaging) and on (B) axial gadolinium-enhanced T₁ weighted imaging. CISS, constructive interference in steady state; HRT₂W-MRI, high-resolution, T₂ weighted MRI.

washout period of 2 weeks before the images were reallocated to the observers. This process was repeated until measurements had been provided using both techniques by each observer. A third random allocation occurred to ensure that 20 patients had intraobserver data collected for both Gd-MRI and HRT₂-MRI.

Statistical analysis

Paired student *t*-tests ($\alpha = 0.05$) were used to determine whether differences in the mean tumour measurements between HRT₂W-MRI and Gd-MRI were statistically significant. Intra- and interclass correlation coefficients were calculated to determine intra- and interobserver concordance. Coefficient values above 0.9 indicated excellent concordance, those between 0.75 and 0.9 good concordance, 0.5 and 0.75 moderate concordance and those under 0.5 poor concordance.¹² Bland–Altman plots were used to evaluate the level of agreement between *vs* measurements obtained on HRT₂W-MRI and Gd-MRI.¹³ All statistical analyses were performed using IBM SPSS Statistics (v. 22, IBM Corp, Armonk, NY).

National data gathering

Consultant neuroradiologists within the 30 adult neurosurgical units in the UK (according to those listed by The Society of British Neurological Surgeons¹⁴) were contacted via email and asked to provide the MRI protocol used for the surveillance of non-operated *vs* in their institution.

Economic comparison between Gd-MRI and HRT₂-MRI

The cost to the MRI department in Leeds Teaching Hospitals NHS Trust for a single scanning episode for surveillance *vs* imaging using protocols with Gd-MRI and with HRT₂W-MRI was determined.¹⁵ The number of patients scanned in Leeds Teaching Hospitals NHS Trust for surveillance of non-operated *vs* over a 1 year period (1

July 2016–30 June 2017) was derived from radiology records using the local radiology information solution (CRIS™ Healthcare Software Solutions Ltd, England & Wales). Total MR image acquisition time for HRT₂-MRI and for Gd-MRI protocols was sought.

RESULTS

Patient demographics

Of the 50 patients, 26 were female. Median age was 65 years (range 42 to 88).

The grades of *vs* according to Koos classification were as follows: *N* = 20 Grade I; *N* = 13 Grade II; *N* = 9 Grade III; and *N* = 8 Grade IV.

Imaging findings

There was no statistically significant difference in the mean diameter of *vs* size, measured on HRT₂W-MRI and Gd-MRI for both neuroradiologists (Observer 1 and 2) (Table 1).

Interobserver concordance between the neuroradiologists demonstrated excellent correlation (Table 1 and depicted graphically in Figures 2 and 3).

Intraobserver concordance was similarly excellent (Table 2).

Bland–Altman plots and subsequent linear regression analysis ($p > 0.05$) showed the differences between the two sequences were within limits of agreement for both observers, indicating that the HRT₂W-MRI and Gd-MRI methods could be used interchangeably (Figures 4 and 5).

MRI protocols across the UK neuroscience centres
26 of 30 adult UK neuroscience centres responded to the email request to provide their institutional protocol for the

Table 1. Mean tumour size for $HR T_2 W$ -MRI and Gd-MRI, as measured by the two neuroradiologists (Observer 1 and 2) & interobserver concordance for $HR T_2 W$ -MRI and Gd-MRI. p values > 0.05 indicate no statistically significant difference between the mean of the tumour measurements on $HR T_2 W$ -MRI and Gd-MRI for both neuroradiologists. Interclass correlation coefficient (ICC) of 0.99 indicates excellent inter observer concordance between the neuroradiologists

	$HR T_2 W$ -MRI $N = 50$	Gd-MRI $N = 50$	P value (CI)
Observer 1 Mean TR (mm) $\pm$ SD	13.3 $\pm$ 6.3	13.1 $\pm$ 6.7	0.28 (-0.16 to 0.53)
Observer 2 Mean TR (mm) $\pm$ SD	13.6 $\pm$ 6.3	13.6 $\pm$ 6.5	0.74 (-0.35 to 0.25)
ICC (CI)	0.99 (0.988 to 0.996)	0.99 (0.980 to 0.998)	

CI, confidence intervals; $HR T_2 W$ -MRI, high-resolution, T_2 weighted MRI; SD, standard deviation; TR, transverse diameter of the tumour.

p -values > 0.05 indicate no statistically significant difference between the mean of the tumour measurements on $HR T_2 W$ -MRI and Gd-MRI for both neuroradiologists. Interclass correlation coefficient (ICC) of 0.99 indicates excellent interobserver concordance between the neuroradiologists.

Figure 2. Scatter plot graphical depiction of inter observer correlation on measuring vs on $HR T_2 W$ -MRI. $HR T_2 W$ -MRI, high-resolution, T_2 weighted MRI.

surveillance of non-operated *vs*, giving a response rate of 87%. From the 26 centres that responded, 16 (62%) use Gd-MRI as part of the imaging protocol. 10 (38%) centres do not use Gd-MRI and instead use $HR T_2$ -MRI. 6 of the 16 centres that use Gd-MRI also include a $HR T_2$ -MRI sequence within the surveillance protocol.

Of the 16 adult UK neuroscience centres that use Gd-MRI as part of their protocol for the surveillance of non-operated *vs*, 3 do this using volume pre- and post-gadolinium (2 centres whole brain, 1 centre limited to the posterior fossa). The other 13 centres typically perform axial and coronal T_1 weighted imaging pre- and post-gadolinium through the internal auditory meatus. 3 from these 13 centres perform their post-gadolinium imaging with fat saturation.

Figure 3. Scatter plot graphical depiction of inter observer correlation on measuring vs on Gd-MRI.

Table 2. Intraobserver concordance for HRT₂W-MRI and Gd-MRI

	Observer 1		Observer 2	
	HRT ₂ W-MRI N = 20	Gd MRI N = 20	HRT ₂ W-MRI N = 20	Gd MRI N = 20
First measurement Mean TR (mm) ± SD	12.7 ± 5.9	12.8 ± 6.6	13.4 ± 6.1	13.2 ± 6.1
Second measurement Mean TR (mm) ± SD	12.2 ± 6.0	12.5 ± 6.5	13.3 ± 6.1	12.9 ± 6.2
ICC (CI)	0.98 (0.95 to 0.99)	0.99 (0.97 to 0.99)	0.99 (0.97 to 0.99)	0.99 (0.98 to 0.99)

CI, confidence interval; HRT₂W-MRI, high-resolution, T₂ weighted MRI; ICC, intraclass correlation coefficient; SD, standard deviation; TR, transverse diameter of the tumour.

Figure 4. Bland-Altman plot of vestibular schwannoma measurement for Observer 1 using HRT₂W-MRI and Gd-MRI sequences. The values on the x-axis represent the mean of the measurements from the two sequences. The values on the y-axis represent the differences in the measurements from the two sequences. Horizontal lines indicating mean and 95% limits of agreements are also shown. HRT₂W-MRI, high-resolution, T₂ weighted MRI

Economic comparison between Gd-MRI and HRT₂-MRI

In Leeds Teaching Hospitals NHS Trust, the cost to the MRI department for a single scanning episode for surveillance vs imaging with a Gd-MRI protocol is £116.91 compared to

Figure 5. Bland-Altman plot of vestibular schwannoma measurement for Observer 2 using HRT₂W and Gd-MRI sequences. The values on the x-axis represent the mean of the measurements from the two sequences. The values on the y-axis represent the differences in the measurements from the two sequences. Horizontal lines indicating mean and 95% limits of agreements are also shown. HRT₂W-MRI, high-resolution, T₂ weighted MRI.

£80.00 for HRT₂W-MRI.¹⁵ Over a 1 year period (1 July 2016–30 June 2017), Leeds Teaching Hospitals NHS Trustour institution scanned 516 patients for the surveillance of non-operated *vs*. Based on these data, the utility of HRT₂-MRI rather than Gd-MRI could provide a potential saving of nearly £37.00 per imaging episode, equating to £19,092 per year but this is likely an underestimate when further savings on cannulation procedures are taken into account. The HRT₂-MRI protocol takes 7 min to acquire compared to 18 min for the Gd-MRI.

DISCUSSION

This study has demonstrated the following: (1) variance in MRI protocols for the surveillance of *vs* across the UK; (2) HRT₂-MRI is cheaper than Gd-MRI for the surveillance of *vs* and; (3) a high concordance between HRT₂-MRI and Gd-MRI used for the measurement of non-operated *vs*.

This study supports the use of HRT₂W-MRI alone for the surveillance of non-operated *vs* rather than using Gd-MRI. The average size and location of *vs* in this study were comparable to other studies.^{8,16} Whilst some studies have utilised volumetric measurements of *vs*,⁸ we chose to employ a single linear measurement as we felt that this technique is more easily applicable to the clinical reporting arena and is therefore more likely to be utilised by radiologists. The literature is also supportive of using linear dimension rather than volumetric calculations.^{17–20} Furthermore, the method utilized to measure *vs* in this study (using the inbuilt calliper software in PACS) offers reproducibility to other healthcare centres.

The high intra- and interobserver concordance shown here are comparable to other published studies. A recent American-based study by Coelho *et al* reported correlation coefficients between HRT₂W-MRI and Gd-MRI of 0.991 and 0.973 for neuroradiologists 1 and 2 respectively, with no statistically significant differences between the imaging techniques.⁷ A Turkish group,⁸ also demonstrated a very high level of correlation between two observers when assessing for growth of *vs* using HRT₂W-MRI. Correlation provides valuable information about concordance of the test but does not confirm whether a new test should replace an existing proven method. This requires a measurement of agreement which can be tested with Bland–Altman plots.¹³ The present study demonstrates agreement between the two sequences (HRT₂W-MRI and Gd-MRI) when measuring *vs* irrespective of the level of neuroradiology experience (3 years versus 12 years). Mean biases for each observer were considered clinically acceptable with an underestimation of 0.05 mm (Observer 2) and an overestimation of 0.19 mm (Observer 1) using HRT₂W-MRI when compared to Gd-MRI and with the limits of agreements falling around ± 2 mm. Similar limits of agreement have been shown in previous research that have compared measurements of *vs* using Gd-MRI to HRT₂W (i.e. +2.67 to –2.1 mm, +1.96 SD to –1.96 SD).⁸ It should be emphasized that any change from using Gd-MRI to HRT₂-MRI would produce a measurement of a *vs* that could then be used as a comparator reference for subsequent surveillance imaging with follow-up HRT₂-MRI. As we have proven high concordance between Gd-MRI and HRT₂-MRI there should be no statistically

significant change when moving from a surveillance programme with Gd-MRI to a surveillance programme with HRT₂-MRI.

This study particularly adds to the literature by highlighting the variation in MRI surveillance practice throughout the UK. 62% of the UK neuroscience centres are still utilizing Gd-MRI. As such, patients under surveillance are exposed to repeated injections of gadolinium-based contrast agents which is not without risk. The administration of gadolinium (a rare paramagnetic metal) is associated with allergic reactions and systemic toxicity such as nephrogenic systemic fibrosis.²¹ More recently, gadolinium has been shown to accumulate in body tissues, including the brain and especially in the globus pallidi and dentate nuclei.²² The exact effects of this deposition are yet to be fully elucidated but, the neuronal deposition is thought to be dose-dependent, suggesting that efforts should be taken to reduce unnecessary exposure to gadolinium injection.¹⁶

In addition to the possible health benefits by switching from Gd-MRI to HRT₂W-MRI, there are also potential financial savings. *vs* surveillance imaging with HRT₂W-MRI is nearly £37.00 cheaper per imaging episode than Gd-MRI. This is not insignificant, especially when extrapolated to over 500 patients within Leeds Teaching Hospitals NHS Trust that undergo surveillance of non-operated *vs* per year. With the HRT₂W-MRI protocol taking almost one-third of the time of the Gd-MRI protocol extra scanning capacity could also be created. Moreover, by applying the principles of Getting It Right First Time (GIRFT) and harmonizing a surveillance protocol across the NHS, it may be possible to make substantial savings, particularly when data from this study suggest that 16 (from the 26 responding) adult neuroscience centres still use Gd-MRI in *vs* surveillance protocols, meaning savings could run into hundreds of thousands of pounds each year. With patient safety of paramount importance and in this time of increasing health economic scrutiny, consideration must be given to alternative safer and less-expensive diagnostic and surveillance imaging techniques without sacrificing outcomes.

The authors recognize that this study has limitations, including it is retrospective, it was performed in a single centre with a relatively small sample size and subset analysis of differences between Gd-MRI and HRT₂W-MRI with respect to Koo's classification was not performed. Furthermore, in Leeds Teaching Hospitals NHS Trustour institution patients are allocated to MRI according to availability on the hospital MR scanners with machines historically optimized for SPACE or for CISS depending on the time of installation and the machine capability. Both CISS and SPACE sequences are routinely used interchangeably in the investigation of cisternal pathology, and for this study were assumed to provide equivalent contrast between soft tissue and CSF. Subsequently subset analysis between the two sequences was not performed.

HRT₂W-MRI is also not without its limitations. Its sensitivity and specificity in the detection of cerebellopontine angle lesions range from 77 to 100% and 94 to 98% respectively.^{8,23–26} Small lesions may be overlooked leading to false-negative results. Alternatively, false-positive claims can be caused by a vascular

structure or inflammatory mimic. These challenges do not apply to this study as we have only examined patients with known vs. However, it would suggest that there is still a requirement for gadolinium-enhanced imaging in the setting of possible vs. We would advocate the screening of vs with HRT₂-MRI and in equivocal cases an additional Gd-MRI could be performed to confirm. HRT₂-MRI (rather than Gd-MRI) could then be used for future surveillance.

Before implementing a change in practice, it is important to consider the wider implications. The decision should be multidisciplinary, taking into account the thoughts of other stakeholders such as the ear, nose and throat surgeons and neurosurgeons. Moreover, patients will need to be consulted, especially those patients who have been undergoing surveillance using Gd-MRI. It will be important to substantiate the change based on scientific research and not merely as a cost-saving mechanism. Some patients that are grounded in the system may associate a change with substandard care enforced by financial constraints. There may also be a requirement to explain that contrast-enhanced MRI remains safe, so that scaremongering does not ensue. A change

in practice may also benefit from a wider discussion within the NHS so that national guidelines for vs surveillance can be generated with consideration to the utility of HRT₂-MRI. There are also other areas of surveillance imaging that may oblige the need for Gd-MRI, for instance in the follow-up of meningiomas and pituitary adenomas. Further research into these areas and a wider discussion on their widespread clinical applicability in the NHS would seem pertinent.

CONCLUSION

This study highlights the variation in imaging protocols used in the surveillance of vs across the UK neuroscience centres with the majority of centres using Gd-MRI. It also demonstrates high concordance between HRT₂W-MRI and Gd-MRI in the measurements of vs, suggesting that the use of HRT₂W-MRI alone could provide an alternative to Gd-MRI for the surveillance of non-operated vs—an alternative that is more cost-effective and of reduced risk to patients. A larger multicentre, multireader study should be considered to validate these findings prior to implementing a nationwide change in practice.

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