In vivo pre-operative magnetisation transfer ratio for detection of thyroid malignancy

Sidhartha Nagala[1], Mary McLean[2], Piyush Jani[1], and John Griffiths[2]
[1]*Otolaryngology, Addenbrooke's Hospital, Cambridge, United Kingdom,* [2]*Cambridge Research Institute, Cancer Research UK, Cambridge, United Kingdom*

Introduction

The current gold standard for screening of thyroid tumours is ultrasound-guided needle biopsy, an operator-dependent technique. Even if the operator is experienced and the sample is sufficient for diagnosis, the false negative rate for cancer can vary from 1% to 6% (1). Hence, there is a need for new additional screening tests.

Magnetisation transfer (MT) imaging measures the reduction in signal from free water protons after application of a pulse to saturate immobile protons (bound to macromolecule proteins). One study found a lower MT ratio in excised thyroid follicular carcinomas compared to follicular adenomas *in vitro* (2). It was hypothesised that this was due to carcinomas having lower colloid content. Colloid is the fluid contained in thyroid follicles, predominantly composed of the glycoprotein, thyroglobulin. We present the results of the first study investigating this technique pre-operatively in patients with thyroid tumours.

Methods

27 patients with suspected thyroid tumours requiring surgery and 5 normal subjects underwent MT imaging on a 3Tesla HDx scanner (GE Healthcare, Waukesha WI, USA). Signal was transmitted using the body coil and received using two channels of a four-channel phased array surface coil (PACC, Machnet BV, Elde, The Netherlands) designed for studies of the carotid arteries. One arm of the coil was centred over the region of interest to maximize local sensitivity and secured by a soft cervical collar to reduce motion artefact. A locally-modified 3D fast spoiled gradient echo sequence was used for magnetization transfer. The 'MToff' sequence (TE = 2.1ms; TR = 20ms; FOV 24 x 19.2cm; matrix 256x160; 1 average) generated 12 contiguous slices with a slice thickness of 3 or 4mm to cover the whole lesion. The 'MT on' sequence contained an additional 10ms Fermi pulse, with a frequency offset of 2200 Hz and a nominal flip angle of 360°. The MT images were processed using an in house program written in IDL (ITT Visual Information Solutions, Boulder, CO, USA). Magnetization transfer ratio (MTR) parameter maps were calculated as:

$$MTR = 1000 * (1 - MTon / MToff) \quad (3)$$

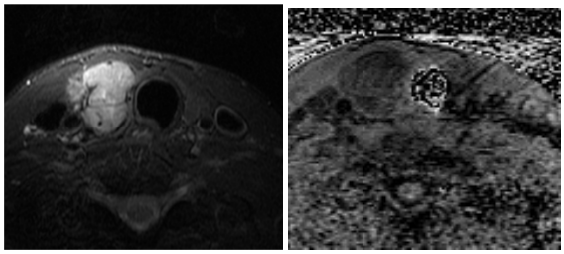
The pixel intensities of the MT maps were therefore equal to the MTR in units of tenths of a percent. Pixels in the MT maps were set to 0 anywhere they were below 0 or the initial intensity of the MTon images was 0, to avoid amplification of noisy data. ROIs were drawn with reference to the T2-weighted images (TE = 102ms; TR = 3780ms; FOV 18; matrix 384x256; 2 averages; 15 slices, slice thickness 5mm, spacing 1 mm) (see example in Fig. 1), avoiding cysts and areas of strong susceptibility artifact. Subjects with a low maximum signal intensity (<1000) over the ROI in the MToff images were rejected for analysis, since this suggested suboptimal coil placement. Severely distorted images which resulted in an inability to reliably determine a ROI were also rejected. In Image-J (National Institutes of Health, USA), ROIs were defined in either tumour (see example in Fig. 1), nearby muscle, or normal thyroid tissue (in controls). Mean MTR values normalised to muscle were calculated using Image-J for each ROI and multiple slices were averaged. Values were correlated to postoperative histological diagnosis.

Results and Discussion

25/27 thyroid lesions and 5/10 normal thyroid lobes were satisfactory for MT analysis. Postoperative histology revealed 12 malignant tumours, 9 benign tumours and 4 nodular goitres. A one way ANOVA test showed a significant difference ($p = 0.0005$) for normalised mean MTR values between normal, benign and malignant thyroid tissue (see Fig. 2). Using a MTR cut off value of 0.47, overall sensitivity and specificity for detection of malignancy in suspected thyroid tumours were 82% (95% confidence interval [CI] 48-98%) and 90% (CI 56-99%), respectively. Positive predictive value and negative predictive value were 90% (CI 56-99%) and 82% (CI 48-98%) respectively. The area under the ROC curve (see Fig. 3) was 0.81 (CI 0.54-1.08, $p = 0.017$). This indicates the test does discriminate between benign and malignant thyroid tumours.

Conclusion

Our results indicate that preoperative MT imaging is a promising new screening test for malignant thyroid nodules. In future we will investigate the added value of combining it with other imaging techniques to improve pre-operative characterization of thyroid nodules and ultimately reduce the need for repeat surgery.



A: T2- weighted B: MTR map

Figure 1: Example of a malignant thyroid nodule (papillary carcinoma)

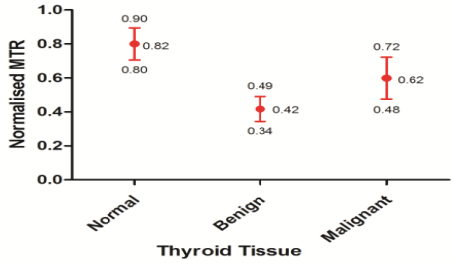


Figure 2: Graph showing mean MTR values as a ratio of muscle MTR with 95% CIs. (Difference between means are statistically significant)

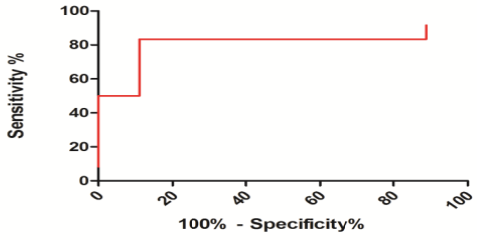


Figure 3: ROC curve for detection of thyroid malignancy in suspected thyroid tumours using MT imaging (Area under curve 0.81)

References

1) Mazzaferri EL, N Engl J Med. 328: 553-9 (1993).
2) Callicott C & Goode AW, Phys Med Biol. 43 (3): 627-35 (1998).
3) Dousset V et al., Radiology. 182 (2): 483-91 (1992).