Any abnormal growth of thyroid cells into a lump within the thyroid is commonly referred to as a thyroid nodule. Thyroid nodules are most common endocrine tumors having a reported prevalence of 4 - 7% in the adult population and are sonographically detected in 30 - 50% of the population. In Pakistan where goiter is endemic in certain areas, thyroid cancer is responsible for 1.2% cases of all malignant tumors. The female to male ratio in this part of the world is noted to be between 2.5 - 4:1, which is comparable to international data.

Data about the use of MR imaging in the diagnosis of thyroid cancer has been inadequate owing to the relative recent development and limited use of this technology in many parts of the world. This is due to the technical difficulties in obtaining good MR image quality in the head and neck regions as the anatomic heterogeneity of the area, with adjacent air and bone, gives rise to susceptibility artifacts and also due to the motion artifacts caused by respiratory and swallowing movements. However, with subsequent developments, these problems have been overcome thus creating new possibilities. Diffusion-weighted MR imaging (DWI) is non-invasive and does not involve administration of contrast or radiation exposure. It provides image contrast through measurement of the diffusion properties of water within tissues. It is used to differentiate benign and malignant lesions where increased cellularity of malignant lesion restricts water motion in a reduced extracellular space. Structural changes / characteristic of malignant or benign tissue will result in different signals on DWI, which may be quantified by calculating the Apparent Diffusion Coefficient (ADC). Several diagnostic tests such as scintigraphy, ultrasonography and Fine Needle Aspiration Cytology (FNAC) have been used to differentiate benign from malignant thyroid nodules pre-operatively. The advantage of Magnetic Resonance Imaging (MRI) in this context is its lack of invasiveness with ability to show precise anatomical detail better than any other imaging modality.

INTRODUCTION

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ABSTRACT

Objective: To determine the diagnostic accuracy of Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) mapping in differentiating benign from malignant thyroid nodules by taking histopathology as the gold standard.

Study Design: A cross-sectional analytical study.

Place and Duration of Study: Department of Radiology at Combined Military Hospital (CMH), Lahore, from August 2012 to July 2013.

Methodology: Thirty-five patients, who were referred to radiology department of CMH, Lahore, for ultrasound or Fine Needle Aspiration Cytology (FNAC) of thyroid gland, fulfilling the inclusion and exclusion criteria, were included in the study. They were evaluated on 1.5 Tesla MRI machine with T1- and T2-weighted imaging as well as fat-suppressed technique. DWI was done using b-values of 0 and 1000 s/mm² and ADC values were calculated for the thyroid nodules. All of these patients were subjected to ultrasound guided core biopsy and histopathology results were correlated with ADC values.

Results: The benign nodules showed facilitated diffusion while malignant nodules showed restricted diffusion. T-test was used to assess the difference in mean ADC values between benign and malignant nodules. The mean ADC value of the malignant thyroid nodules (0.94 ±0.16 x 10⁻³ mm²/s) was significantly lower than that of the benign thyroid nodules (1.93 ±0.13 x 10⁻³ mm²/s) (p-value < 0.05). ADC value of 1.6 x 10⁻³ mm²/s was used as a cut-off, for differentiating benign from malignant thyroid nodules. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of DWI and ADC values in differentiating benign from malignant thyroid nodules were 93%, 95%, 93%, 95% and 92.3%, respectively.

Conclusion: DWI is a non-invasive diagnostic tool for characterization and differentiation between benign and malignant thyroid nodules. It not only decreases the burden of unnecessary surgeries when pre-operative FNAC and biopsy are inconclusive, but is also helpful in reaching a definite diagnosis when a nodule is not amendable to biopsy due to any reason.

Key Words: Diffusion weighted imaging (DWI). ADC mapping. Thyroid nodules. MRI.
The rationale of the present study was to obtain sufficient data\textsuperscript{7} supporting the accuracy of DWI through calculated ADC values in differentiating between benign and malignant thyroid nodules, helping in developing future non-invasive and objective management protocol. Although international studies are available,\textsuperscript{7-10} Pakistani data is lacking in this regard.

The objective of this study was to evaluate the role of DWI in differentiating benign from malignant thyroid nodules using histopathology as gold standard.

**METHODOLOGY**

This analytical study was conducted at Department of Radiology at Combined Military Hospital (CMH), Lahore, from August 2012 to July 2013.

Patients of either gender aged 20 - 65 years, having thyroid nodules referred to the Radiology Department of CMH, Lahore for ultrasound or FNAC of thyroid gland, were included. The exclusion criteria were thyroid nodule which was purely cystic or measured less than 9 mm on ultrasound; with evidence of thyroiditis clinically and on ultrasound or with recent radiotherapy of the neck for any reason or FNAC/biopsy of thyroid within less than 3 weeks prior to MRI examination or any MRI-incompatible metallic device in their body, or having tremors or uncontrollable cough as they would cause motion artifacts in the MRI examination and claustrophobic patients.

After permission from the Hospital Ethical Committee, 35 patients were included in the study fulfilling the inclusion and exclusion criteria. MRI was done after taking written informed consent from the patients and objective of the study was explained to every subject to be included in the study. Demographic data, including name, age, sex and contact number, was also obtained.

MRI including DWI was performed on 1.5 Tesla MRI machine (Achieva SMI 2.5, NOVA Dual; Philips Medical Systems) keeping the patient in supine position with a dedicated head and neck coil around him/her. The conventional MR imaging protocol for thyroid was followed by diffusion weighted imaging using b-values of 0 (b\textsubscript{1}) and 1000 s/mm\textsuperscript{2} (b\textsubscript{2}).

For quantitative analysis of tissue-specific diffusion capacities, the ADC value was calculated by placing region of interest in solid portion of nodule excluding its cystic part. The ADC values are expressed in square millimeters per second. ADC maps and analysis of the histogram were generated off-line with a pixel-by-pixel method. The difference between the ADC values of benign and malignant nodules was noted. Collected data was analyzed with computer software SPSS version 20.0, medical diagnostic test calculator and GraphPad QuickCalc t-test calculator. Frequency, mean and standard deviation were also computed for ADC values, histopathological results, diffusion pattern and age. A 2 x 2 contingency table and medical diagnostic calculator were both utilized to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of DWI/ADC mapping for differentiation of benign from malignant thyroid nodules by taking histopathology as gold standard. The difference between mean ADC value of benign and malignant thyroid nodules was tested using t-test. A p-value < 0.05 was considered to indicate a statistically significant difference.

**RESULTS**

Thirty five patients with 64 thyroid nodules were included in the study. Eighteen patients had solitary thyroid nodules, 9 patients had two nodules, 5 had three thyroid nodules, 2 had four and 1 patient had five thyroid nodules. The mean size of the nodules was 1.5 ± 0.7 cm with their sizes ranging from 1.0 to 3.6 cm. Twenty-one patients had benign (Figure 1) and 14 had malignant nodules (six papillary carcinomas, five follicular carcinomas (Figure 2), one oncocytic follicular carcinoma, one Hurthle cell carcinoma and one lymphoma) according to the histopathology results. Confidence intervals (CI) of 95% were evaluated for ADC values. The mean ADC value of the malignant thyroid nodules was 0.94 ± 0.16 x 10\textsuperscript{-3} mm\textsuperscript{2}/s (ranged from 0.78 to 1.1 x 10\textsuperscript{-3} mm\textsuperscript{2}/s) (Figure 3) and mean ADC of the benign nodules was 1.3 ± 0.2 x 10\textsuperscript{-3} mm\textsuperscript{2}/s.

![Figure 1: Benign follicular adenoma showing facilitated diffusion and high ADC value.](image)

![Figure 2: Follicular carcinoma showing restricted diffusion with low ADC value.](image)
thyroid nodules was $1.93 \pm 0.13 \times 10^{-3} \text{ mm}^2/\text{s}$ (ranged from $1.80$ to $2.06 \times 10^{-3} \text{ mm}^2/\text{s}$, Figures 1, 2 and 3). The sensitivity, specificity, PPV, NPV and diagnostic accuracy of DWI in differentiating benign from malignant thyroid nodules were $93\%$, $95\%$, $93\%$, $95\%$ and $92.3\%$, respectively. However, it was not possible to differentiate amongst different types of carcinomas.

**DISCUSSION**

Thyroid nodules are the commonest disorder presenting to an endocrine surgeon and have a high sonographic prevalence in general population.4,6 Though the majority of the thyroid nodules are benign, however, it is prudent to differentiate the benign from malignant ones in order to decrease the risk of unnecessary surgery for the benign thyroid nodules, as well as the financial burden to the community. DW-MRI provides a non-invasive and fairly accurate means for achieving that, with added advantage of evaluating local disease extension and metastatic spread owing to the superior anatomical detail offered by this modality.

Malignant thyroid nodules showed a restricted pattern of diffusion with a reduced ADC value $(0.94 \pm 0.16 \times 10^{-3} \text{ mm}^2/\text{s})$ while the benign thyroid nodules showed a facilitated pattern of diffusion with higher ADC value $(1.93 \pm 0.13 \times 10^{-3} \text{ mm}^2/\text{s})$. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of DWI in differentiating benign from malignant thyroid nodules were $93\%$, $95\%$, $93\%$, $95\%$ and $92.3\%$, respectively.
contrary, Schueller-Weidekamm et al. reported that malignant lesions had a high ADC value attributing it to the increased number and size of macrofollicles filled with colloid; thus the motion of water protons is increased. This leads to an increased diffusion capacity and high ADC values. The ranges of the ADC values for carcinoma were 2.4 - 3.0 x 10^{-3} \text{ mm}^2/\text{s} and adenoma 1.63 - 2.2 x 10^{-3} \text{ mm}^2/\text{s} using b-values of 0 and 800. However, most of the studies do not share this interpretation.

In this study, anatomical delineation was improved using the fat-suppressed technique. Good image quality for diffusion weighted images was obtained by using a high b-value of 1000 s/mm² as a higher b-value reduces the influence of perfusion on DWI. This is shown by the high SNR on DWIs in these images. Consequently, the ADC values, in fact, are indicating the diffusion capacity in normal and abnormal thyroid tissue without being markedly influenced by perfusion. The use of sagittal as well as coronal DW images, as compared to just the conventional axial scans, assisted in improved placement of ROI. Single shot navigated echo planar technique was used for DWI which reduced image acquisition time and artifacts.

The limitations of the study include inability to predict malignancy in lesions smaller than 9 mm in size, thus missing the micro-carcinomas, completely remove motion and breathing-related artifacts despite recent improvements and presence of intra-lesional bleed or calcification altering the ADC value.

In future, there is a possibility of detecting even small carcinomas by using higher spatial resolution with a smaller voxel size (< 0.5 mm³) and evaluation by MR imaging machine of more than 3-Tesla strength.

CONCLUSION

DWI is a promising non-invasive diagnostic modality for characterization and differentiation of benign and malignant thyroid nodules of > 9 mm in size with the benign nodules showing facilitated diffusion while malignant nodules showing restricted diffusion. It not only reduces the unnecessary surgeries when pre-operative FNAC and biopsy are inconclusive but is also helpful in reaching a definite diagnosis when a nodule is not amenable to biopsy due to its small size or if the patient is unwilling for it. It can also help in nodule selection thus increasing the yield of FNAC/biopsy when malignancy is suspected.

REFERENCES


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