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Normal pituitary and microadenoma T1 signal measurements: A retrospective investigation using DCE MRI signal time curves

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***Abstract*---**Background: The most often used technique for detecting pituitary microadenoma is dynamic contrast enhanced magnetic resonance imaging (DCE MRI). However, the high rate of false positivity in its interpretation is a problem due to differential amplification of the normal pituitary. Purpose: The purpose of this study was to see if the precontrast T1 signal intensity ratio (SIR) of lesions identified on DCE MRI could be used to predict the existence of microadenoma. Materials and Methods: We looked at the MRIs of 23 patients who were referred for DCE MRI of the pituitary gland (group 1, 15 patients with diagnosis of pituitary microadenoma; and group 2, patients not clinically labelled as microadenoma). STC were plotted, and T1 SIR was acquired at t = 0 s at the suspect zone of differential augmentation (SIR T) and normal pituitary (SIR P). For each patient, the SIR difference (SIR P SIR T) and relative SIR difference (SIR P SIR T/SIR P) were calculated and compared between the two groups. Results: Patients with microadenoma have a lower mean T1 SIR than those without (P = 0.065). Patients with microadenoma had a greater SIR difference and relative SIR difference (P = 0.003 and 0.005, respectively). According to Receiver Operated Characteristic Curve Analysis, a cutoff of 26 and 0.107 for SIR difference and relative SIR difference, respectively, could identify microadenoma with 100% specificity and acceptable sensitivity. Conclusion: The STC curve-derived baseline precontrast T1 SIR

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evaluation of a lesion thought to be a microadenoma on DCE MRI can improve diagnostic confidence in microadenoma identification.

***Keywords*---**dynamic contrast, magnetic resonance imaging, pituitary microadenoma, signal time curve.

Introduction

The baseline precontrast T1 SIR evaluation of a lesion suspected of being a microadenoma on DCE MRI using the STC curve can improve diagnostic confidence in microadenoma detection. The backbone of pituitary imaging, magnetic resonance imaging (MRI), has essentially replaced computed tomography (CT) for the identification and localization of microadenomas. Although spin echo (SE) MR sequences were the first to be used in the identification of pituitary adenoma, their sensitivity was low, particularly in cases of microadenoma. [2,3] Following investigations revealed that microadenoma identification improved with contrast studies and was time dependent after contrast injection. Early dynamic scan was proposed to improve the contrast between the normal gland and the microadenoma. [4:06] The use of dynamic pituitary MRI during contrast scanning has boosted diagnostic yield for these lesions and is now the gold standard. Increased false positivity is a significant issue with dynamic MRI. [2, 3, 7, 8] At this time, no one MRI sequence has been found to be unambiguously effective in detecting them, therefore diagnosis is based on a mix of images collected before, during, and after the contrast injection. [9]. Through signal time curve (STC) analysis, this study aimed to combine the benefits of precontrast T1 SE sequence with dynamic contrast enhanced magnetic resonance imaging of the pituitary gland in the evaluation of microadenoma. We wanted to see if evaluating the precontrast T1 signal intensity ratio (SIR) of a suspicious lesion seen on DCE MRI could help with microadenoma localization.

Materials and Methods

Patients

The institutional review board (IRB) approved this study, and each patient participating in it gave their informed permission. We looked at the MRI pictures of 23 patients who were sent for dynamic postcontrast MRI of the pituitary gland. These patients were separated into two groups for our research. Group 1 (n = 15; male/female ratio, 4:11; mean age, 36 years) consisted of 15 patients who were labeled as pituitary microadenoma in clinical records based on compelling clinical and biochemical evidence compatible with adenomas. In all these patients, MRI had reported a focus of differential enhancement sized 3–10 mm in the pituitary gland on dynamic contrast study suggestive of microadenoma. Of these, 11 were labeled as prolactinomas, who had galactorrhea, infertility, or amenorrhea with serum prolactin >50 ng/mL. Acromegaly was found in four of these patients, with growth hormone levels above 20 ng/mL in four of them.

Group 2 (n = 8; male/female ratio, 1:7; mean age, 34 years) included eight individuals who were not diagnosed with microadenomas after undergoing

hormonal testing and an MRI scan. Seven of these patients had complained of galactorrhea, amenorrhea, or infertility, but their serum prolactin levels were still less than 26 ng/mL. One male patient was being tested for a bulky pituitary that had been reported by an outside institute, but he was later diagnosed with hypothyroidism. In six of these patients, the MRI was described as a normal scan. A focus of differential enhancement on dynamic contrast testing in two of these patients was worrisome for adenoma, according to MRI.

MR protocol

All patients had their MRIs done using a 1.5 Tesla Siemens Avanto system with an actively shielded whole body superconducting magnet (Siemens Avanto, Erlangen, Germany). A 20-channel head–neck coil was used for imaging. For the assessment of pituitary and brain morphology, a coronal precontrast VIBE sequence with TR/TE of 497/10 ms, 320× 320 matrix, 230 mm Field of view (FOV), and 2.5 mm slice thickness without gap was acquired. After the precontrast process, a coronal dynamic contrast scan was performed with a 15 mm FOV, 3 mm slice thickness, and 0.2 mm slice gap utilising the rapid SE sequence. When the first dynamic stopped and the second began, contrast was inserted. The dynamic series lasted 225 seconds and included one precontrast dynamic and six cycles during and after contrast injection. At a rate of 2 mL/s, 10 mL of 0.01 mmol/kg gadopentetate dimeglumine (Magnevist; Bayer HealthCare Pharmaceuticals, Wayne, NJ) were administered.

MRI analysis

For the group 1 patents, our institute's final MRI report was used to determine the tumour location. By studying the MR images, the first author was able to confirm the presence of the lesion. Forced choice required a senior radiologist with 15 years of experience to highlight a focus of decreased signal in dynamic contrast pictures and to specify whether an adenoma could be present in the images for group 2 patients. The radiologist was not blinded to the final clinical diagnosis but was blinded to the MRI data. He noted suspicious areas of differential enhancement in two of the eight patients, which he said were evident in two or more of the successive postcontrast enhancements. In the remaining six patients, a differential enhancement (lowest signal) area was delineated for investigation in a single image.

In all of the patients in groups 1 and 2, a region of interest (ROI) was drawn on the focus of differential enhancement (zone a). A second ROI was drawn on all of the patients in pituitary gland tissue that seemed normal (zone b). As per the established institutional protocol, signal intensity time curves were created in all of the patients at both of these locations. Three parameters were recorded for each patient:

- Baseline T1 SIR at 0 s at suspicious zone (zone a) of differential enhancement (SIR T) and at normal pituitary (zone b) (SIR P)
- SIR difference: SIR P − SIR T
- Relative SIR difference: The ratio of the SIR difference divided by the SIR of normal pituitary = (SIR P − SIR T)/ SIR P.

- The negative values, if any, for SIR difference and relative SIR difference was ignored for calculation of mean.

Statistical analysis

SPSS software was used to conduct the statistical analysis (IBM Corp 2013. Version 22.0. Armonk, NY). The first stage involved comparing the mean of all three parameters between groups 1 and 2 using the independent sample Mann–Whitney U test. The second step involved creating a receiver operated characteristic (ROC) curve for these three variables in order to predict the presence of microadenoma.

Results

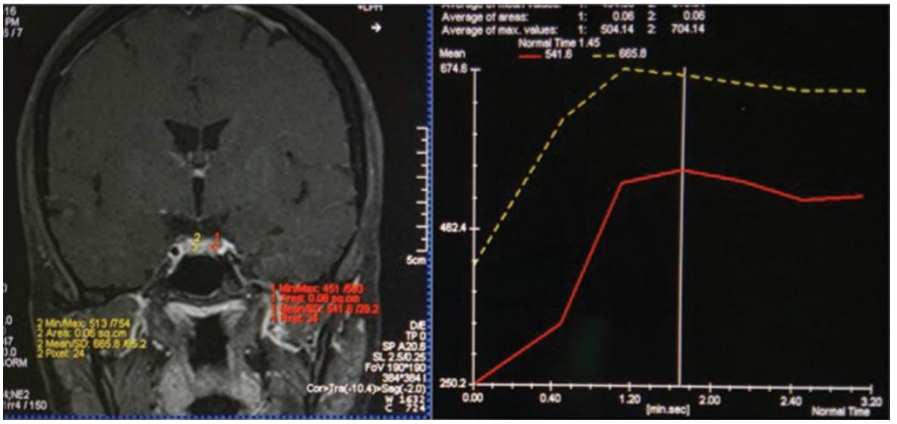

Figure 1. Demonstrates placement of ROI within the normal appearing anterior pituitary gland (yellow) and microadenoma (red). Corresponding signal-time curve shows that there is significant difference enhancement between the microadenoma and normal pituitary and difference in precontrast signal at t = 0 s

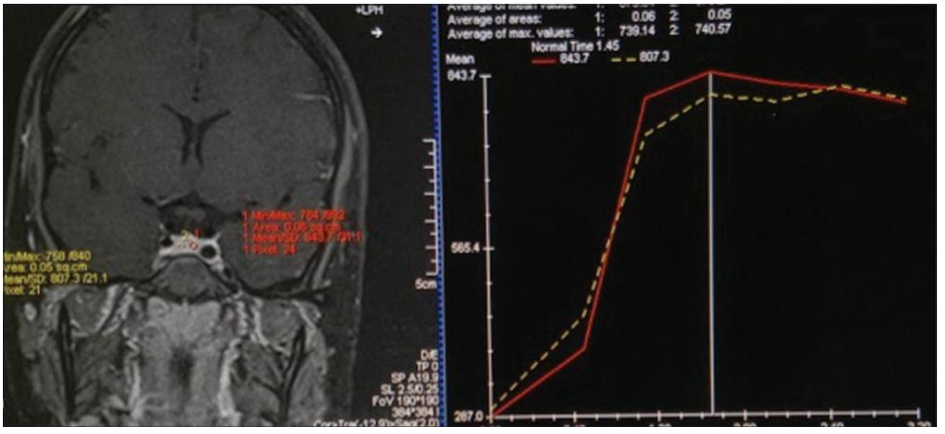

Figure 2. Dynamic MRI of a 24-year-old female patient in group 2, presenting with galactorrhea. ROI placed in normally enhancing anterior pituitary (red) and an area of differential decreased signal (yellow) is shown and the corresponding

signal–time curves show that the suspicious area shows almost similar (and slightly higher) baseline T1 signal at t = 0 s

In group 1 [Figure 1] and group 2 patients [Figure 2], STC from ROI placed over the normally enhancing anterior pituitary and suspicious area of differential enhancement revealed that 14 out of 15 cases of group 1 (with microadenoma) had lower baseline T1 signal intensity compared to the normal anterior pituitary. One patient, who was being treated for prolactinoma with bromocriptine, had a little larger T1 signal than a normal pituitary. Six of the eight patients in group 2 had a lower T1 signal than the normal pituitary, while two had a greater T1 signal than the normal pituitary.

Table 1
Mean, standard deviation, and comparison of the mean values of three parameters between two groups using Independent-sample Mann-Whitney *U*-test

Parameters	Group 1 (n = 15)		Group 2 (n = 8)		P
	Mean	SD	Mean	SD	
Baseline T1 SIR value	285.13	48.6	331.13	50.79	0.065
SIR difference	95.07	111.84	12.25	8.97	0.003
Relative SIR difference ratio	0.215	0.205	0.037	0.028	0.005

SIR= Signal intensity ratio

Table 1 summarises the mean values, standard deviations, and results of the independent sample Mann–Whitney U test used to compare mean values between the two groups for the three parameters. Although the difference was not significant (P = 0.065), patients with a diagnosis of microadenoma (group 1) had a lower mean baseline T1 SIR. Group 1 had a substantially greater difference in baseline T1 SIR between the normal pituitary and the zone of concern (SIR difference) (P = 0.003). The relative SIR difference between cases and controls was similarly considerably larger in cases (P = 0.005).

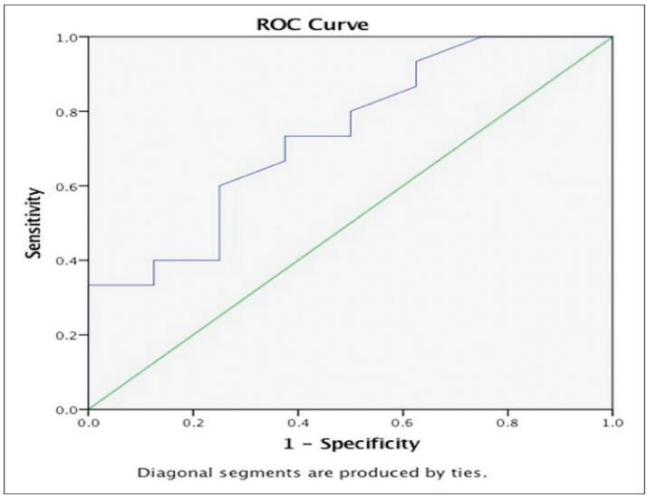

Figure 3. Receiver-operated characteristic curve of the baseline T1 signal if the suspicious lesions in prediction of presence of microadenoma

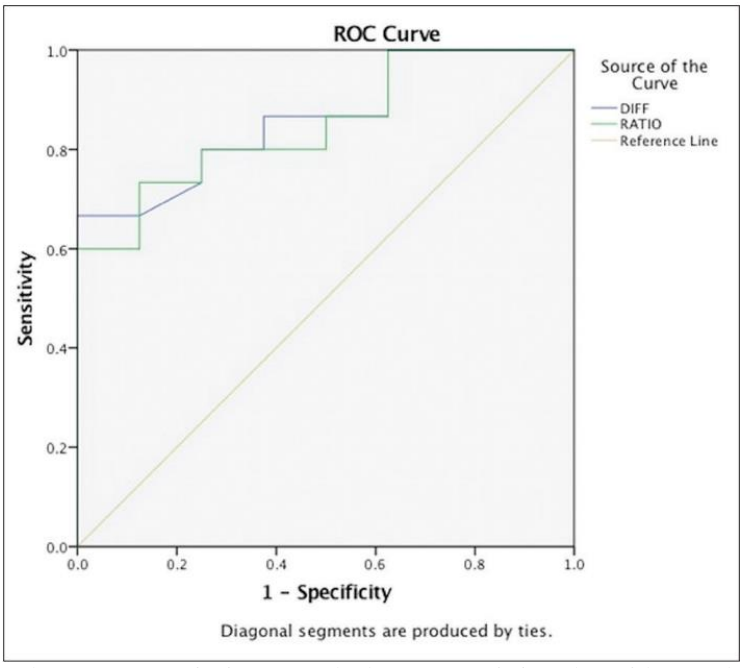

Figure 4. Receiver-operated characteristic curve of the signal intensity ratio (SIR) difference (blue) and relative SIR difference ratio (green) in prediction of presence of microadenoma

The area under the curve for all three parameters is large in the ROC curve generated to predict the existence of microadenoma [Figures 3 and 4]. The findings of the ROC curve analysis for the three parameters are summarised in Table 2. The SIR difference has the largest area under curve, followed by the Relative SIR difference.

Table 2
Receiver-operated characteristic curve drawn to predict the presence of micro adenoma for baseline T1 SIR values, its difference from normal pituitary SIR, ratio (difference/SIR of normal pituitary)

Test parameter	Area under curve	Cut off value	Sensitivity (%)	Specificity (%)	Cut-off with 100% specificity	Sensitivity of cut off with 100% specificity (%)
Baseline T1 SIR value	0.738	312	66.7	62.5	-	-
SIR difference	0.863	21	73.3	75	26.5	66.7

Relative SIR difference ratio	0.850	0.057	80	75	0.107	60

SIR= Signal intensity ratio

We discovered that a value of 312 for baseline T1 signal predicts microadenoma with intermediate sensitivity and specificity, based on ROC curves. With excellent sensitivity and specificity, a SIR difference of 21 and a relative SIR of 0.057 between the normal pituitary and the area showing differential enhancement suggested microadenoma. More crucially, with tolerable sensitivities, we were able to achieve a specificity of 100 percent for cut off values of 26 and 0.107 of SIR difference and relative difference, respectively.

Discussion

DCE MRI is now the most often used technology for detecting pituitary microadenomas. The majority of prior research investigating DCE MRI for microadenoma detection relied on subjective visual judgement to distinguish these lesions. Microadenoma is a low-signal region in the anterior pituitary that measures 3–10 mm on dynamic post contrast imaging. The issue with this method is that it has a higher rate of false positives. [2,3] Because of the varied blood supply, the pituitary often shows uneven contrast enhancement. On a single picture, a lower contrast enhancement area can be misconstrued as an adenoma. Furthermore, the accuracy of the diagnosis is dependent on the interpreting radiologist's experience, and there are no objective diagnostic criteria. Few studies have attempted to evaluate STCs on DCE MRI to assess time course of enhancement of tumors and the normal pituitary, enabling an increased diagnostic confidence. One such study was conducted by Yuh *et al.*, who concluded that pituitary adenoma enhanced 9.3 ± 1.5 s after straight-sinus enhancement and significantly (12.0 s) before anterior pituitary enhancement.[10] Rossi Espagnet *et al.*, were first to study STCs of the pituitary in 52 patients to establish optimum acquisition time for microadenoma detection and concluded that 120 s is ideal time for imaging.[11] They also found out that there was significant difference in peak enhancement of microadenoma and normal anterior pituitary. Moreover, pituitary microadenoma showed mean time-to-peak of 90 s, whereas normal anterior pituitary showed an earlier peak enhancement with mean time-to-peak of 80s.

Stadnik *et al.* compared DCE MRI and precontrast T1 images in 12 patients with microadenoma and found that both T1 sequence and DCE MRI was able to detect 84% (10/12) lesions, whereas the combination of both dynamic MRIand precontrast T1 sequence was able to detect 100% of cases.[12] Ma *et al.* in his study observed that a significant correlation between tumor consistency and expression of collagen IV was seen with signal intensity on precontrast T1 SE sequences.[13] In our study, 14 out of 15 cases of microadenoma revealed lower signal intensity compared with the normal anterior pituitary. While in one patient, who was on bromocriptine therapy for prolactinoma, showed mildly higher T1 signal than normal pituitary. This result was in concordance with the previous studies that showed that most of the microadenoma demonstrates increased T1

and T2 relaxation times. One of the initial studies has reported atypical T1 and T2 relaxation signals in patients with bromocriptine and attributed this to loss of cell volume owing to medical therapy.[14]
Our study demonstrated that difference of T1 SIR of the normal pituitary and the lesion under consideration is significantly high in patients with pituitary microadenoma than those without. The SIR difference and the relative SIR difference were able to predict the presence of microadenoma with 100% specificity with reasonable sensitivities. A difference of T1-SIR of 26.5 between the lesion and the normal pituitary and a relative SIR difference ratio of 0.028 were able to predict the presence of microadenoma in all the cases. The findings of the present study have great implication while interpretation of DCE MRI and we speculate that addition of these parameters can reduce false positivity rate that has been one of the major criticisms of DCE MRI.

Our study utilizes the combined merits of dynamic contrast properties as well as internal relaxation properties of microadenomas for their diagnosis. Moreover, this study provides quantitative parameters that can be reliably used to increase the diagnostic confidence of DCE MRI in diagnosing pituitary microadenoma. Small sample size and lack of surgical and histopathological evidence were the major limitations of this study. Moreover, owing to its retrospective nature, we could not perform T1 mapping of pituitary, which could further validate our concept. Also, presence of nonfunctioning adenomas in the control group could not be excluded as the clinical diagnosis was considered gold standard in the present study and surgical evidence was lacking. Last, interpreting radiologist in our study was not blinded to the clinical picture that can lead to patient selection bias. We recommend future multicentric prospective studies having larger sample sizes with an effort to reduce selection bias and histopathological confirmation to validate the results of our study.

Conclusion

In conclusion, our study demonstrated that assessment of baseline precontrast SIR derived through STC of the pituitary microadenoma, suspected on dynamic contrast MRI, can increase diagnostic confidence in their diagnosis and localization. Moreover, we have shown that the quantitative assessment would be more meaningful if interpreted with the SIR of an internal reference, i.e., normal appearing pituitary gland.

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