The success of MRI in preoperative detection of primary hyperparathyroidism focus and contribution to other imaging methods

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Purpose

Primary hyperparathyroidism (PHPT) is a disease characterized by excessive secretion of parathyroid hormone. The incidence of disease is approximately 0.1-0.3% in general population (1). The most common cause of PHPT is a single parathyroid adenoma (80-85%). Other causes are pair adenomas (2-5%), parathyroid hyperplasia (10-15%), parathyroid carcinoma (1%), parathyroid cysts (<1%) (2, 3, 4, 5). 4-16% of parathyroid glands are located ectopically (6).

Surgery is the only curative treatment in PHPT patients. There is no need for determination of preoperative localization of the lesion in traditional neck exploration. The gold standard technique is traditional bilateral neck exploration (BNE). The first BNEs have a success rate over 95%, when they are performed by experienced surgeons. But, after recurrent neck explorations, success rates decrease to 60% with high complication rates and morbidity. However, in recent years, minimally invasive parathyroidectomy (MIP) which increases the comfort of surgeon and patient, has become a new standard in many institutions. MIP needs preroperative localization of the lesion (7, 8, 9).

In recent studies, a multimodality approach is aimed to develop for preoperative localization of parathyroid diseases in order to help surgery (10, 11).

The purpose of this study is to assess the success of MRI in detecting preoperative localization of PHPT focus in the lights of latest technical developments and literature and investigate the contribution to other imaging modalities.
Methods and materials

Between June 2008 and May 2013, we retrospectively analyzed 159 parathyroid lesions of 150 patients who have been considered as PHPT as the result of laboratory tests and clinical signs, and prediagnosed as parathyroid pathology after MRI, US, $^{99m}$Tc MIBI, SPECT and SPECT/CT. All patients underwent surgery and the diagnoses were proven pathologically. 6 patients needed second operation due to recurrency and persistency.

All patients' serum parathyroid hormone (PTH), total Ca, ionized Ca, phosphor (P), 25-hydroxy vitamin D (25-OH vitamin D) and creatinine levels were measured before and after surgery. PTH and calcium levels in normal ranges were confirmed after operation.

MRI examination was performed in all patients. All images were acquired from a 1,5 Tesla (T) MR scanner (GE 450W 32 CH with IROC Optima, USA) and an 16 channel neurovascular coil (HNS NV full,USA, 2009). Parameters are given in table (Table 1). Hypervascular parathyroid adenomas (PA) are usually iso-hypointense on T1W images, hyperintense on T2W images. They show rapid arterial enhancement after Gadolinium (GD-DTPA) injection.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Coronal T1A FSE</th>
<th>Coronal STIR</th>
<th>Axial T1A FSE</th>
<th>Axial T2A FSE</th>
<th>Sagittal STIR</th>
<th>Coronal +C T1A IDEAL</th>
<th>Axial+C T1A FSE</th>
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<td>TR/TE</td>
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<td>3400/12</td>
<td>625/4</td>
<td>3000/19</td>
<td>3000/12</td>
<td>590/3</td>
<td>625/4</td>
</tr>
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<td>ETL</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td>19</td>
<td>12</td>
<td>3</td>
<td>4</td>
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<td>31</td>
<td>41</td>
<td>41</td>
<td>31</td>
<td>62</td>
<td>41</td>
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<tr>
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<td>4/0,5</td>
<td>4/0,5</td>
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<td>4/0,5</td>
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<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>
Tablo 1. Sequence parameters of MRI. FSE fast spin-echo, STIR short tau inversion recovery IDEAL iterative decomposition of water and fat with echo asymmetry and least squares estimation, TR time to repeat, TE time to echo, ETL echo train length, BW bandwidth, FOV field of view, ST/SR Slice thickness/Section range, NEX Number of excitation

US (Log#q 9, GE Healthcare, Milwaukee, WI, USA) with linear transducers (5-12 MHz) were used in all patients. ⁹⁹mTc MIBI were used in all patients too. ⁹⁹mTc MIBI-SPECT (Nucline Spirit DHV-S, Mediso Co., Budapest, Hungary, 2008) were used in 73 lesions and ⁹⁹mTc MIBI-SPECT/CT (GE Hawkeye, DH gama camera, GE Healthcare) in 85 patients.

SPSS for Windows 11.5 were used for data analysis. Kolmogorov Smirnov test, Student's t test, Mann Whitney U test, Pearson chi-square and Fisher chi-square tests were used for statistical analysis. Sensitivity, specificity, positive and negative predictive values and accuracy rates were calculated. The significance level was 0.05.
Results

One-hundred and fifty patients were included to study. 28 patients were male and 122 patients were female. The median age was 55.5 (range, 27-80 years).

All patients were operated. MIP was applied for 72 patients (45.3%), BNE for 78 patients (49.1%) and unilateral NE for 9 patients (5.7%).

Parathyroid lesions were classified as normal/ectopic located, solitary/pair, hyperplasia, re-operated. Success rates of imaging methods were calculated.

Totally 159 parathyroid lesions were analysed. Parathyroid tissue was found in 132 (83%) of them, but no parathyroid tissue was observed in 27 (17%) lesions (Table 2).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of lesions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pathology: Lesion (+)</strong></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>132 (83.0)</td>
</tr>
<tr>
<td>PA (Parathyroid adenoma)</td>
<td>126 (79.2)</td>
</tr>
<tr>
<td>PH (Parathyroid hyperplasia)</td>
<td>5 (3.2)</td>
</tr>
<tr>
<td>PC (Parathyroid carcinoma)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Solitary lesion</td>
<td>114 (71.7)</td>
</tr>
<tr>
<td>Pair lesion (Bilateral and 2)</td>
<td>18 (11.3)</td>
</tr>
<tr>
<td>Normal located (right-left sup-inf)</td>
<td>121 (76.1)</td>
</tr>
<tr>
<td>Ectopik lesion (sup med.,intrathymic,intrathyroidal)</td>
<td>11 (6.9)</td>
</tr>
<tr>
<td><strong>Pathology: Lesion (-)</strong></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27 (17.0)</td>
</tr>
<tr>
<td>Parathyroid tissue</td>
<td>14 (8.8)</td>
</tr>
<tr>
<td>LN (Lymph node)</td>
<td>8 (5.0)</td>
</tr>
<tr>
<td>Thyroid tissue</td>
<td>4 (2.56)</td>
</tr>
<tr>
<td>Thyroid nodule</td>
<td>1 (0.64)</td>
</tr>
</tbody>
</table>

Table 2. Distribution of lesions according to pathology.

When single or more imaging techniques were used for investigation of parathyroid lesions, general sensitivity, sensitivity in ectopic lesions and pair adenomas, accurate
detection rates of hyperplasia and re-operated lesions are: MRI: 68.2%; 72.7%; 38.9%; 0% (0/5); 71.4% (5/7), US:80.3%; 54.5%; 50.0%; 40% (2/5); 42.8% (3/7), MIBI planar:69.7%; 81.8%; 55.6%; 40% (2/5); 85.7% (6/7), SPECT:68.4%; 80%; 62.5%; 66% (2/3); 50% (1/2), SPECT/CT:86.5%; 87.5%; 81.1%; 50% (1/2); 100% (6/6), MRI +US:90.2%; 81.8%; 72.2%; 40% (2/5); 100% (7/7), MRI+MIBI:82.6%; 90.9%; 72.2%; 40% (2/5); 85.7% (6/7), MRI+SPECT:80.7%; 80.0%; 75.0%; 40% (2/5); 71.4% (5/7), MRI+SPECT/CT:87.8%; 87.5%; 81.8%; 20% (1/5); 85.7% (6/7), US+MIBI:94.7%; 90.9%; 88.8%; 80% (4/5); 85.7% (6/7), MRI+US+MIBI:96.2%; 100%; 94.4%; 80% (4/5); 100% (7/7), MRI+US+MIBI+SPECT:98.2%; 100%; 100%; 100% (5/5); 100% (7/7), MRI+US +MIBI+SPECT/CT:97.3%; 100%; 100%; 80% (4/5); 100% (7/7), respectively.

General sensitivity, specificity, diagnostic accuracy rates of MRI were found similar with MIBI and MIBI-SPECT. Similar sensitivity values were also found in preoperative, re-operated and ectopic lesions. No parathyroid hyperplasia was detected on MRI. Sensitivity of MRI was significantly lower in pair adenomas. However, interestingly, MRI detected lesions in different locations in which other modalities were not able to detect (3 ectopic lesions that US couldn't detect, 1 ectopic lesion that MIBI couldn't detect, 4 pair lesions that US couldn't detect, 3 pair lesions that MIBI couldn't detect, 4 lesions in re-operated patients that US couldn't detect and 1 lesion that MIBI couldn't detect). There are parathyroid adenomas in normal locations (Figure 1, 2, 3), in ectopic locations (Figure 4, 5) and adenomas with atypical signals (Figure 6, 7) in our cases.

When evaluations were combined; common sensitivity rates were found 96.2% on MRI+US+MIBI. Sensitivity in ectopic lesions was found 100% on MRI+US+MIBI. Pair lesion sensitivity was 100% on MRI+US+MIBI (and/or SPECT SPECT/CT). Hyperplasia sensitivity was 100% on US+MIBI (and/or SPECT SPECT/CT). MRI+US sensitivity was found 100% in re-operated patients. Sufficient clinical performance was provided with these sensitivity rates.
Fig. 1: 50-year-old female patient. Parathyroid lesion adjacent to posteroinferior of left thyroid lobe. US: Hypoechoic lesion showing peripheral low flow pattern on color Doppler US.

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Fig. 2: 50-year-old female patient. Parathyroid lesion adjacent to posteroinferior of left thyroid lobe. MRI: Parathyroid lesion outside thyroid parenchyma. Intermediate signal on T1W, hyperintense on T2W, enhancement after contrast injection.

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**Fig. 3:** 50-year-old female patient. Parathyroid lesion adjacent to posteroinferior of left thyroid lobe. MIBI, SPECT ve SPECT/CT: Focal pathologic activity retention in inferior part of thyroid left lob.

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**Fig. 4:** 37-year-old female patient. MRI: Superior mediastinal lesion with 9x6 mm in size, located in tracheal bifurcation plane. Hypointense on T1W, hyperintense on T2W, enhancement after contrast injection.

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**Fig. 5:** 37-year-old female patient. MIBI, SPECT, SPECT/CT: Focal activity retention under right manibrium sterni.

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Fig. 6: 74-year-old female patient. MRI: Intrathyroidal lesion in right lobe. Hyperintense component on both T1W and T2W images due to hemorrhage.

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Fig. 7: Same patient in Figure 6. MRI: Nodular lesion, 28x21x19mm in size, extending from the vicinity of thyroid right lobe to superior mediastinum. Slightly hyperintense on T1W, hyperintense on T2W, peripheral enhancement after contrast injection (hemorrhagic atypical parathyroid adenoma).

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Conclusion

Minimally invasive surgery methods which increase the comfort of surgeons and patients, directed the researchers to preoperative localization studies (1, 12, 13). The aim of the radiologist in preoperative localization is to identify all abnormal parathyroid tissue, localize it and provide the information needed for preoperative planning to the surgeon (14). MRI offers high spatial resolution and excellent soft tissue contrast. MRI allows noninvasive evaluation of organ functions by measuring blood flow and tissue perfusion. All parathyroid abnormalities can be viewed with detailed anatomic information (mandibular angle, superior mediastinum). Therefore MRI has great potential in diagnosis of parathyroid adenoma (15, 16).

In literature, MRI sensitivity is between 63-77%\(^{15,16,17-19}\) in overall, 40-100%\(^{7,20,21-23,24-28}\) in ectopic lesions, 0%\(^{24-37,5,29}\) in multiple adenomas, 0%\(^{24-42,3-75}\)\(^{18,20,29}\) in hyperplasias, 75-89%\(^7,21\) in re-operated patients. Overall sensitivity of MRI has similar rates in pre-operative, re-operated and ectopic lesions. But sensitivity is decreased in hyperplasias. There are few studies related to multiglandular disease and MRI sensitivity is very low in these studies. In our study, sensitivity of MRI is consistent with literature in overall, ectopic lesions, pair adenomas and reoperated lesions. No hyperplasia was detected by MRI in our study.

MRI features of parathyroid adenomas are closely associated with histology (10). Hypervascular adenomas are usually iso-hypointense on T1W images, hyperintense on T2W images. They show rapid enhancement after Gadolinium (Gd-DTPA) injection (15, 30, 31). These typical characteristics may not be seen in 30-40% of adenomas (7, 10, 20). Parathyroid adenomas may be seen iso-hypointense on T1 and T2W images secondary to cellular degenerative changes, old hemorrhage and fibrosis. They may be seen hyperintense on T1 and T2W images secondary to acute-subacute hemorrhage, cystic degenerative changes (31-33). We had one parathyroid lesion (hemorrhagic intrathyroidal lesion) detected only by MRI.

Primary diagnosis methods in preoperative localization of parathyroid adenomas are US in radiology and MIBI in scintigraphy (41). SPECT and SPECT/CT provide functional and anatomic information complementary to planar imaging on MIBI (10). Overall sensitivity values in literature are 76%\(^{34}\) for US, 78.2%\(^{10}\) for MIBI, 78.9%\(^{10}\) for SPECT, 96.7%\(^{35}\) for SPECT/CT. There is consistence between literature and our study. US sensitivities have been found reduced in ectopic lesions (especially mediastinum), multiple adenomas, hyperplasia and reoperated patients (2,3,10,12,14,16,21,27,29,36,37). Interestingly, we detected more mediastinal lesions (54.5%). MIBI sensitivity for re-operated and ectopic lesions is similar to the overall sensitivity. Decreased MIBI sensitivities were reported in multiple adenomas and hyperplasia (3, 12,14,16,29,33,36). In our study, MIBI sensitivity for re-operated and ectopic lesions is higher than the overall sensitivity. MIBI sensitivity
for pair lesions and hyperplasia were lower but US and MIBI complemented each other by detecting patients in different categories. Combined use of imaging techniques increased sensitivity compared with single use, in detecting preoperative localization of abnormal parathyroid glands (16, 32, 38). Combinations increased sensitivity in our study too.

MRI and CT indications for parathyroid lesions are similar (11, 14). In recent years, sensitivity of 4D-CT was found 89.4% in detecting parathyroid adenomas and positive predictive value was found 93.5% in PHPT patients (US sensitivity 76%, MIBI-SPECT 78.9%, same study) (34). The most important problem is high radiation dose in 4D-CT (increased thyroid cancer risk in young female patients, no higher risk in older patients), 57 times higher than MIBI (39). 4D-CT should not be used as primary diagnostic method in young patients because of high radiation dose. 4D-CT was reported as a valuable method in elderly patients, re-operated patients and ectopic parathyroid lesions which could not be detected by other modalities (2, 39).

Detection rates of preoperative localization of parathyroid lesions increased due to technical developments in MRI. Allison et al. used 3T MRI in PHPT patients and have found parathyroid lesions (4/7, 57%) which were not detected by MIBI (15). Aschenbach et al. have found dynamic MR angiography more sensitive and more specific ((93.3% and 100%, respectively) than conventional MRI and MIBI. Unlike MIBI, four adenoma and large lymph nodes have been detected by MR angiography (32). MRI diffusion and spectroscopy have not been studied yet.

Phased algorithm system is proposed in the surgical management of PHPT patients when preoperative localization has to be done (10,37,40,41,42). Most common approach is US and $^{99m}$TcMIBI (+SPECT) in first-diagnosed and re-operated patients. If definitive diagnosis couldn't be made by US and/or $^{99m}$TcMIBI, especially in mediastinal lesions, 4D-CT may be considered in older patients and MRI in young and older patients (11, 40). In the lights of the latest technical developments, we think that MRI may be an alternative method to CT for preoperative localization of parathyroid lesions. US and MRI combination should be preferred in young people and pregnant due to lack of radiation risk.

There are some limitations of our study. Statistical analysis couldn't be performed in recurrent-persistent PHPT and patients with hyperplasia due to small number of patients. MIBI-SPECT and MIBI-SPECT/CT couldn't be applied to all patients, so statistical analysis were performed with available data. Because of insufficient number of histopathological data, statistical analysis couldn't be performed for lesion size.

As a result; preoperative imaging methods used in PHPT may change according to the patient and hospital conditions. Conventional MRI has similar sensitivity with MIBI and MIBI-SPECT in terms of detection of preoperative localization. Eventhough conventional MRI is not the primary method used in preoperative and operated cases,
when US and MIBI are insufficient, especially in the detection of ectopic lesions, accuracy rates increase with the use of MRI.
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