4D MRI for the Localization of Parathyroid Adenoma: A Novel Method in Evolution

Shlomo Merchavy, MD¹,², Judith Luckman, MD³, Michal Guindy, MD, MPA³, Yoram Segev, MD³, and Avi Khafif, MD¹

No sponsorships or competing interests have been disclosed for this article.

Abstract
The sestamibi scan (MIBI) and ultrasound (US) are used for preoperative localization of parathyroid adenoma (PTA), with sensitivity as high as 90%. We developed 4-dimensional magnetic resonance imaging (4D MRI) as a novel tool for identifying PTAs. Eleven patients with PTA were enrolled. 4D MRI from the mandible to the aortic arch was used. Optimization of the timing of image acquisition was obtained by changing dynamic and static sequences. PTAs were identified in all except 1 patient. In 9 patients, there was a complete match between the 4D MRI and the US and MIBI, as well as with the operative finding. In 1 patient, the adenoma was correctly localized by 4D MRI, in contrast to the US and MIBI scan. The sensitivity of the 4D MRI was 90% and after optimization, 100%. Specificity was 100%. We concluded that 4D MRI is a reliable technique for identification of PTAs, although more studies are needed.

Keywords
4D MRI, parathyroid adenoma, Sestamibi scan, ultrasound, minimally invasive surgery

Received June 19, 2015; revised October 14, 2015; accepted October 29, 2015.

The incidence of primary hyperparathyroidism (PHPT) is 0.2% to 0.5% in the general population.¹ The most common cause of PHPT is sporadic solitary adenoma (85%), followed by 4-gland hyperplasia (9%) and double adenoma (3%).²,³ In the last decade, due to the high sensitivity of the ultrasound (US) and sestamibi (MIBI) scan (>90%),⁴ bilateral neck exploration is currently being replaced by minimally invasive parathyroidectomy (MIP).⁴,⁵ MIP is associated with benefits of limited cervical dissection, smaller surgical incision, less postoperative pain, and decreased cost due to reduced hospital lengths of stay.⁵,⁶ Although US and MIBI scan are reliable modalities, there are cases in which they fail to demonstrate the adenoma. Other modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI), have demonstrated low sensitivity and specificity and therefore are not routinely used in patients with PHPT with negative US or MIBI scans.³ Four-dimensional (4D) CT was lately reported as an effective tool in identifying hidden adenomas,⁷ but it is associated with high radiation exposure.

We developed a new MRI protocol: 4D MRI as a novel tool for identifying parathyroid adenoma.

Methods
This study was approved by the local ethics committee of Assuta Medical Center, Tel Aviv, Israel. Patients were enrolled in the study if they underwent MIP in the Assuta Medical Center between September and November 2014. All patients had localization of the adenoma by US and MIBI scan prior to surgery. MRI was performed on a 1.5-T Espree Siemens machine. Standard sequences were performed, including T1 and T2 TSE axial sequences and T2 MEDIC sequences (GE T2), from the mandible to the thoracic inlet, as well as coronal and sagittal and coronal T1 and STIR. A dynamic study was performed. For the first 4 patients, different dynamic magnetic resonance angiogram sequences were performed, including TWIST and bolus studies. The resolution in these sequences was inadequate to differentiate between the adenoma and the surrounding soft tissues. Therefore, the protocol was adjusted. The final technique used was 1.5-mm T1 vibe sequences (GE T1) in axial planes, scanned in dynamic fashion every 13 seconds for 10 times, starting without contrast and continuing with a gadolinium contrast that was injected by an automatic injector. Rate of injection was 4 mL/s with a total of 12 to 20 mL of Gadovist (gadobutrol) or Dotarem (gadoterate meglumine), depending on patient weight. The imaging

¹ARM Center of Otolaryngology Head and Neck Surgery, Assuta Medical Center, Tel Aviv, Israel
²Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel
³Imaging Department, Assuta Medical Center, Tel Aviv, Israel

This article was presented at the 2015 AAO-HNSF Annual Meeting & OTO EXPO; September 27-30, 2015; Dallas, Texas.

Corresponding Author:
Shlomo Merchavy, MD, Department of Otolaryngology—Head and Neck Surgery, Padeh Medical Center, 15208 Poriya, Israel.
Email: Merchavy@gmail.com
studies were analyzed by a dedicated head and neck neuroradiologist who was blinded to the US and MIBI scan results.

Surgery was terminated when 2 parameters were achieved: histologic finding of hypercellular parathyroid gland on frozen section reading and decrease of intraoperative parathyroid hormone levels (>50%) 10 minutes after removal.

**Results**

Eleven patients (8 women) aged 37 to 73 years (mean, 58 years) enrolled in the study after undergoing successful removal of parathyroid adenoma by MIP, with subsequent normalization of calcium and parathyroid hormone levels. Parathyroid adenomas were identified by 4D MRI in all except 1 patient (false negative). As mentioned, due to inadequate resolution and 1 false negative (9%) among the first 4 patients, the protocol was adjusted, and fast T1 vibe sequences (GE T1) in the axial plane were obtained before injection and every 13 seconds for 10 sequential scans. Adenomas were visualized on the static images (Figure 1) and dynamic scans and demonstrated fast enhancement after 26 to 30 seconds (Figure 2). False positives did not occur after optimization.

In 9 patients, there was a complete match between the 4D MRI and the US and MIBI and with the operative finding. In 1 patient, the US and MIBI wrongly identified a left thyroid nodule as a parathyroid adenoma. However, during surgery, the adenoma was identified on the right side, as shown by the 4D MRI.

The positive predictive value of the 4D MRI was 91%. In the final protocol, after optimization, sensitivity was 100%.

**Discussion**

In our study, we found that 4D MRI is a reliable diagnostic tool for the evaluation of parathyroid adenoma.

To enable MIP, accurate localization is required. US and MIBI scans are the main imaging modalities and commonly used in combination to localize the diseased gland.

US is a noninvasive, inexpensive tool to localize parathyroid adenoma. However, its sensitivity and specificity are controversial, since they are operator dependent. Siperstein et al reported a US sensitivity of 65% to 74%.8 In our study, US sensitivity was 91%. Our findings agree with Zawawi et al9 and Bachar et al,3 who reported a sensitivity of 90% and concluded that an experienced radiologist can precisely locate parathyroid adenoma in 90% of patients with PHPT.

The MIBI scan was reported to have high sensitivity and specificity. Our findings agree with Denham et al,4 who reported 90% sensitivity. Still, the MIBI scan has several limitations, since thyroid nodules or other hyperactive metabolic tissues (eg, metastatic lymph node) may mimic parathyroid tissue. The MIBI scan, even when incorporated with
single-photon emission CT, does not always give a detailed anatomic localization of the adenoma and will rarely reveal a double adenoma or hyperplasia of 4 glands. As mentioned, 4D CT has recently been reported as a novel tool to identify hidden parathyroid adenoma.\textsuperscript{7,10} Table 1 compares 4D CT and 4D MRI.

If the results of the US and MIBI scan disagree or if one of the modalities did not localize the adenoma, further imaging modalities are usually preformed (CT, MRI, angiography). In this article, we describe a new 4D MRI protocol as another option for identification of adenomas not found by US, MIBI scan, or both.

### Conclusion

A new tool for identification of parathyroid adenomas was developed. Although initial results are promising, more studies are needed to compare 4D MRI results with surgical findings in patients with negative MIBI and US.

### Author Contributions

Shlomo Merchavy, design the study, analyzed the data, writing the manuscript. approval of final version of manuscript, agree to be accountable for all aspects of the work; Judith Luckman, writing the manuscript and data analysis, critically reviewing manuscript. approval of final version of manuscript, agree to be accountable for all aspects of the work; Michal Guindy, study design conception, critically reviewing manuscript. approval of final version of manuscript agree to be accountable for all aspects of the work; Yoram Segev, study design conception, writing the manuscript, critically reviewing manuscript, critically reviewing the manuscript, agree to be accountable for all aspects of the work.

### Disclosures

**Competing interests:** None.

**Sponsorships:** None.

**Funding source:** None.

### References


### Table 1. Comparison of 4D MRI vs 4D CT.

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<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td>MRI</td>
<td>High sensitivity and specificity</td>
<td>Contraindications: pacemaker, severe claustrophobia, metallic foreign body</td>
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<tr>
<td></td>
<td>No radiation exposure</td>
<td>Experienced neuroradiologist required</td>
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<tr>
<td>CT</td>
<td>Claustrophobia is not contraindicated in CT</td>
<td>Experienced neuroradiologist required</td>
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<tr>
<td></td>
<td>Fewer artifacts due to shorter time of examination</td>
<td>More artifacts due to motion and swallowing</td>
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Abbreviations: 4D, 4-dimensional; CT, computed tomography; MRI, magnetic resonance imaging.