Flexible In-Cavity MRI Receiving Coil for Ultrahigh Resolution Imaging of the Pituitary Gland

Siyuan Liu  
University of California, Los Angeles

Kunal S Patel  
University of California, Los Angeles

Sophie Peeters  
University of California, Los Angeles

Jiahao Lin  
University of California, Los Angeles

Aislyn C DiRisio  
University of California, Los Angeles

Harry Vinters  
University of California, Los Angeles

Robert Candler  
University of California, Los Angeles

Kyunghyun Sung  
University of California, Los Angeles

Marvin Bergsneider  
University of California, Los Angeles

Research Article

Keywords: pituitary microadenoma, Cushing's disease, signal-to-noise ratio, radiofrequency coil

Posted Date: May 5th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2880527/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Purpose

Preclinical design and construction of a flexible intra-sphenoid coil aiming for submillimeter resolution of the human pituitary gland.

Methods

Sphenoid sinus measurements determined coil design constraints for use in > 95% of adult patients. Temperature safety parameters were tested. The prototype 2-cm diameter coil was positioned in the sphenoid sinus of cadaveric human heads utilizing the transnasal endoscopic technique that is used clinically. Signal-to-noise ratio (SNR) was estimated comparing the prototype transnasal coil versus a standard clinical head coil. One cadaver pituitary gland was explanted and histologically examined for correlation to the imaging findings.

Results

With the coil positioned directly atop the sella turcica at 0° angle of the B₀ static field, the craniocaudal distance (24 ± 4 mm) was the limiting constraint. Phantom experiments showed a negligible change in temperature at two sites over 15 minutes. The flexible coil was placed transnasally in cadaveric specimens using an endoscopic approach. The image quality was subjectively superior at higher spatial resolutions relative to the commercial 20-channel head coil. An average 17-fold increase in SNR was achieved within the pituitary gland. Subtle findings visualized only with the transnasal coil had potential pathological correlation with immunohistochemical analysis.

Conclusions

A transnasal radiofrequency coil feasibly provides a 17-fold boost in SNR at 3T, providing, in principle, equivalent imaging to a 5T scanner using a standard head coil. The ability to safely improve the quality of pituitary imaging may be helpful in the identification and subsequent surgical resection of small functional pituitary lesions.

INTRODUCTION

Cushing’s disease (CD) is a potentially fatal disorder caused by an adrenocorticotropic hormone (ACTH) – producing pituitary tumor. Standard of care treatment of this disease is surgical excision of the offending tumor, which yields an 80% cure rate [1]. However, this treatment paradigm relies on preoperative identification of the tumor with magnetic resonance imaging (MRI). While the median size of pituitary tumors causing CD is 5 mm [1], a significant percentage are less than 3 mm in size [2]. Given the small size of these functional tumors, clinical MRI protocols cannot visualize the tumor in every case of CD [2, 3]. In such cases without an MRI-identifiable tumor, neurosurgeons must consider surgically “exploring” the anterior pituitary gland [4, 5]. This technique runs the risk of not finding the tumor as well
as permanently damaging the normal gland resulting in hypopituitarism. Surgery for MRI-negative ACTH-producing microadenomas has a low probability (27%) of finding the tumor [6, 7]. Thus, improved spatial resolution and diagnostic quality of pituitary MRI protocols would improve rates of surgical remission and reduce risk of pituitary damage in patients with CD.

Clinical pre-operative pituitary MRI protocols [3] commonly include: 3 Tesla T1 imaging with and without gadolinium contrast with multi-slice 2D turbo spine-echo (TSE, resolution of 0.7 mm × 0.7 mm, slice thickness of 2–3 mm) and 3D magnetization-prepared 180 degrees radiofrequency pulses and rapid gradient echo (MP-RAGE, isotropic voxel of 0.9-1.0 mm) sequences [2]. With these parameters, definitive identification of tumors ≤ 3mm remains a challenge. The limitations of resolution in clinical pituitary imaging stem from an insufficient signal-to-noise ratio (SNR). Two approaches for improving SNR are to: 1) augment the signal with higher field strengths (e.g., 7T MRI) [8] and 2) decrease the distance between the imaging target and receiver coil [9]. Studies on these methods are limited. Success with 7T imaging for pituitary tumors has been limited to case reports [8] as lesions < 4mm in size cannot be reliably detected, and higher $B_0$ fields lead to shorter relaxation times and thus reduce contrast in conventional T1-weighted imaging [10, 11]. With regards to innovations in the receiver coil, Chittiboina et al. [12] adopted a coil apparatus originally designed for endorectal use and demonstrated improvement in SNR when it was placed within the sphenoid sinus of 5 cadavers via a sublabial transsphenoidal approach. Previously, we reported the development of a flexible miniature coil and validated its feasibility using numerical simulations and experimental phantoms [13]. The miniature coil design provided a maximum of 19-fold SNR improvement compared to a commercial Siemens 20-channel Head/Neck coil within a region of interest in the agar phantom study, and can be surgically positioned in close proximity to the pituitary gland through a transnasal approach. Our aim in this pre-clinical study is to further characterize coil performance and SNR improvement for visualizing pituitary tissue within cadaveric specimens.

In this study, we present a 2-cm diameter flexible radiofrequency receiving coil for diagnostic use in endoscopic endonasal transphenoidal surgery for CD. We describe the methodology of the sphenoid sinus preparation and coil placement. We predict the SNR improvements relative to the commercial head coil with electromagnetic simulations and evaluate the SNR improvement in a cadaveric study. We conduct the temperature measurements on a phantom to assess the safety profile of the coil. This pre-clinical study establishes the technique for intraoperative use of the coil in MRI-negative CD patients.

**METHODS**

**Institutional Approval & Resources**

This study was approved by the institutional review board at UCLA. All cadaveric specimens were acquired, processed, and handled under standard protocols under the supervision of the Surgical Science Laboratory at UCLA. All phantom and cadaveric imaging studies were carried out under the supervision of the Translational Research Imaging Center at UCLA.
Sphenoid Sinus Measurements

MPRAGE brain MRI sequences of 50 patients without sellar tumors were included in this analysis. Images from a 3T MRI (Siemens Prisma, Siemens Healthineers, Erlangen, Germany) 3D magnetization prepared radiofrequency pulse rapid gradient echo T1 with and without gadolinium (Gd-DTPA, 0.1 mmol/kg) contrast were downloaded from the PACS server and subsequently de-identified. Using axial slices, the maximum lateral intercarotid distance and maximum distance at sellar face were measured. Using midline sagittal slices, craniocaudal sphenoid distance anterior to the sella, distance from coil to the posterior pituitary gland, and craniocaudal sellar distance were measured.

Coil Design and Construction

Production of a flexible transnasal miniature coil platform was used as the prototype for all studies [Figure 1A]. A 2-cm diameter loop defining the radiofrequency coil was made from a single continuous copper trace (2 mm in width and 17.8 mm in thickness) and attached to a coaxial cable (Siemens Healthineers: 50 Ω, 1.13 mm diameter, 0.22 mm inner conductor diameter, 20 cm length). There were no electrical components directly on the coil, and the tune-and-match components were placed at the end of the 20 cm coil outside the body. The 20-cm cable is short enough avoid any significant current from the body coil during the transmission, while a longer cable would require common mode current chokes along the length of the cable in order to impede the shield current.

Coil Interface Design

To interface the coil with the proprietary Siemens hardware on the MRI scanner (Siemens Prisma 3T) at our institution, a custom-built docking port was constructed via an MCX connector [Figure 1B]. The docking port communicates with a custom 3D-printed circuit box, which houses the electrical pre-amplifier circuit. The circuit box is linked to the coil via a coaxial cable. This circuit has adjustable components needed for tuning and actively decouples the loop in the transmission phase of the pulse sequence. Only the flexible coil loop [Figure 1C] and cable were designed to be inserted transnasally, while the rest of the device is kept outside of the body during scanning. The coil assembly was tuned to a resonance frequency of 123.2 MHz (for 3T imaging), and the impedance was matched. The coil component was coated with Plasti Dip (Plasti Dip Int., Minneapolis, MN, USA) to prevent fluid electrical coupling and for future planned sterilization. This coating was conformal and flexible [Figure 1D].

Electromagnetic simulation setup

Electromagnetic simulation was used to investigate coil performance. In a previous study, we have shown that this coil simulation model can correctly capture the SNR improvement of the local coil compared to a commercial Siemens 20-channel Head/Neck coil [13]. Based on sphenoid sinus measurements, the 5th percentile value of the craniocaudal sphenoid distance was 21.2 ± 0.8 mm. Therefore, a 2-cm diameter surface coil would fit in more than 95% of the patients. The corresponding coil model was developed in COMSOL® Multiphysics (COMSOLAB, Stockholm, Sweden) as previously described [13]. The SNR
improvement factors of the transnasal miniature coil compared to the commercial head coil were estimated based on the simulated normalized effective transverse field $B_{1 \text{xy}}$ at various rotation angles.

**Temperature measurement**

To assess for safety, the transnasal coil was tested for radiofrequency heating by inserting it into a 980 g pork meat phantom within a room maintained at 20°C. The temperature measurements were performed with a benchtop fiber optic thermometer (FOTEMP1-4, Optocon®). The probe was positioned at two different positions inside the meat phantom. One probe was placed right beneath the coil (measuring site S1) and the other one was on the coil trace (measuring site S2). A continuous 15-minute fast low angle shot three-dimensional imaging (FL3D) sequence was performed on the meat phantom during the temperature measurement (TR = 20 ms, TE = 5 ms, FA = 5°). The body coil was used as the transmit coil and the time-averaged RF power was 0.3 W.

**Cadaveric Studies**

Three cadaveric human heads were used to simulate flexible miniature coil placement. A standard endonasal endoscopic approach was carried out to gain unobstructed access to the sella [Figure 3D]. Any sphenoid septations were drilled down. Bone over the sella was not removed. The coil was inserted through a single nare under endoscopic visualization and positioned directly over the sella parallel to the floor [Figure 3F] with the cadaver head facing towards the ceiling. A bovine collagen sponge (HeliSTAT, Integra LifeSciences Corporation, Plainsboro, NJ) [Figure 3E; 3G] was placed in the clival recess and over the coil to limit air-bone interface and associated artifact. The coil wire was secured to the external nare with a 3 – 0 vicryl suture and adhesive. The cadaveric specimen was then transported to the MRI scanner and examined again to confirm that detachment and movement had not occurred during transport.

The prepared cadavers with transnasal coils in place were scanned with Siemens Prisma 3T MRI Scanner via the T1-MPRAGE sequence and Proton Density sequence at varying resolutions (T1: 0.9 mm × 0.9 mm × 0.9 mm; 0.4 mm × 0.4 mm × 0.4 mm; 0.2 mm × 0.2 mm × 0.2 mm (transnasal coil only); PD: 0.7 mm × 0.7 mm × 3 mm; 0.2mm × 0.2 mm × 0.7 mm) [Supplementary Tables 1–2]. T1-MPRAGE sequence is commonly used clinically, while the Proton Density sequence was performed for pixel SNR measurement.

For the head coil, the phase oversampling was enabled to avoid phase wrapping artifacts due to the small field of view. Phase oversampling was unnecessary with the transnasal coil given localized signal. The pituitary gland was segmented into four 3mm regions (a, b, c) defined by proximity to the sella. Segmentation was performed by two independent observers (S.L., K.P.). Signal was found within each region, noise was defined as the standard deviation of the background intensity, and the SNR was calculated as the signal intensity divided by the noise. The mean SNRs within the pituitary gland were calculated for the segmented regions of interest from the high-resolution proton density sequence images and were compared between head coil and transnasal coil.

**Immunohistochemistry**
Following imaging, the pituitary gland was resected en bloc from the cadaveric specimen. The pituitary infundibulum was preserved to orient the anterior/posterior directionality of the specimen, however the right/left laterality was unable to be confirmed after acquisition. The specimen was cut in the coronal plane, formalin-fixed and paraffin-embedded. Hematoxylin/eosin and reticulin stains were used. Pathologic review was carried out by a board certified neuro-pathologist (H.V.) to identify pathologic correlates to imaging findings.

RESULTS

Anatomic sphenoid sinus measurements suggest feasibility of ≤ 2cm transnasal coil diameter

50 patients with available MP RAGE brain MR imaging without sellar tumors or prior sinus surgery underwent measurement of sphenoid sinus parameters. On midline sagittal images [Figure 2A], the average craniocaudal sphenoid distance anterior to the sella was 24 ± 4 mm. The average distance from the planned coil placement to the posterior pituitary gland was 13 ± 2 mm. The average craniocaudal sellar distance was 7 ± 2 mm. On axial images [Figure 2B], the average maximum lateral inter-carotid distance was 27 ± 3 mm. The average maximum distance at the sellar face was 16 ± 4 mm. The distributions of the primary measurements, the craniocaudal sellar distance increased with greater angulation [Figure 2C]. For placement at 0° angle of the B₀ static field, the craniocaudal distance (24 ± 4 mm) was the limiting constraint. We chose one standard deviation at the lesser dimension as the basis for subsequent simulation experiments and the use of the 20 mm flexible transnasal coil. As shown below, slight angulations up to 20° angle did not significantly degrade the coil SNR performance, and therefore we anticipate this size coil could be used in nearly every patient.

Miniature coil simulations predict 20-fold signal-to-noise ratio (SNR) improvement

SNR improvement of the transnasal coil compared to the commercial Siemens 20-channel Head/Neck radiofrequency coil was simulated. The effective transverse field B_{1xy} of the coil was simulated at a 0°, 20°, and 30° coil rotation angle in the sella. Gradient contour plots spatially represent the SNR improvement from use of the miniature coil [Figure 2D]. For a 0° rotation angle (where the coil plane is parallel to the MR scanner headrest), a 20-fold SNR improvement was expected inside an area measuring 6.0 mm × 17.0 mm around the coil and a 10-fold SNR improvement was expected inside an area measuring 15.2 mm × 17.5 mm. These calculations fall within the size of the pituitary gland with pituitary microadenomas (< 10mm tumor + 5mm × 5mm normal pituitary tissue). With coil rotation, there was a decrease in the height of the improved SNR region, but an increase in the width. Simulations with a coil placed at a 20° rotation angle yielded an expected 20-fold SNR improvement in an area measuring 5.8 mm × 18.5 mm around the coil and a 10-fold SNR improvement in an area measuring 15.0 mm × 19.5 mm around the coil. Simulations with a coil placed at a 30° rotation angle yielded an expected 20-fold...
SNR improvement in an area measuring 5.0 mm × 19.5 mm around the coil and a 10-fold SNR improvement in an area measuring 14.3 mm × 20.0 mm around the coil.

**Temperature variation**

With the 2-cm coil in direct contact with the phantom (Fig. 3A-B), the change in temperature during a 15-minute scan was measured to evaluate for safety. With a 0.3 W time-averaged RF power, there was no detectable change in temperature throughout the experiment at two measurement sites [0° change at site 1; 0° change at site 2, Fig. 3C].

**SNR improvements with transnasal coil in cadaveric studies**

Cadaver heads containing the flexible transnasal coil were imaged to compare differences in SNR. The sellar region was also imaged with the clinical Head/Neck coil MP-RAGE sequences with 0.9 mm slice thickness [Figure 4A] and 0.4 mm slice thickness [Figure 4B]. The transnasal coil shows significantly improved resolution of the pituitary soft tissue as compared to the head coil [Figure 4A-C].

SNR calculations were calculated for various regions of interest (ROI) [Figure 4D]. The mean SNR for the most anterior region (Region a) was 48.5 and the furthest region (Region c) was 14.9 [Table 1]. The mean SNR for the entire pituitary gland ROI (Region a + b) was 39.0. The mean SNR for the head coil was 2.3 and was uniform across all ROIs. The transnasal coil demonstrated a maximum of 21-fold mean SNR improvement and an average of 17-fold mean SNR improvement of the pituitary gland compared to the commercial head coil [Table 1].

![Table 1 - SNR comparison for high-resolution MRI](image)

<table>
<thead>
<tr>
<th>ROI</th>
<th>Mean SNR</th>
<th>Head-coil</th>
<th>Improvement factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROI a</td>
<td>48.5</td>
<td>2.3</td>
<td>21.1</td>
</tr>
<tr>
<td>ROI b</td>
<td>39.0</td>
<td></td>
<td>12.8</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>14.9</td>
<td>6.5</td>
<td>3.9</td>
</tr>
<tr>
<td>(ROIs a and b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROI c</td>
<td>14.9</td>
<td>2.3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

SNR (Signal-to-Noise Ratio); ROI (Region of Interest); Note in Fig. 4D for ROI definitions.

**Histological correlation to transnasal coil findings**

In a single cadaver head, transnasal coil images identified a hypointensity not identified on images using the standard head coil [Figure 5A-B]. Following imaging, the pituitary was removed en bloc, sectioned in the coronal plane, paraffin embedded and stained with hematoxylin and eosin as well as reticulin. [Figure 5C-D]. A board-certified pathologist identified a pituitary cyst on histological sections that potentially correlated with imaging findings, although left/right directionality was lost on tissue acquisition and processing.

**DISCUSSION**
In this study, we show the development, feasibility, and SNR improvement of a flexible transnasal coil for imaging of the pituitary gland. Establishing a range of anatomic sphenoid sinus measurements in the general population allowed for the implementation of a 2 cm coil that can be applied to greater than 95% of patients. A coil electromagnetic simulation model was used to predict the SNR improvement of using a transnasal coil compared to a commercial head coil, providing a convenient and time-efficient way to characterize the coil performance in the clinical environment. Moreover, the simulation model can also be useful in selecting the optimal coil size and shape based on the specific anatomy of each patient in future clinical studies.

The safety and feasibility of the coil placement were evaluated for potential clinical use. During the 15-minute scan, no detectable temperature change was found. The average specific energy absorption rate (SAR) during the scan can be estimated by dividing the time-average input RF power by the sample mass [13]. Therefore, the experimental average SAR is well below the guideline value [14]. We demonstrate that the transnasal coil is unlikely to cause thermal damage to the patient and is safe to be used in the clinical environment. In addition, pre-clinical insertion of the coil in a cadaver head was carried out with the subsequent demonstration of 17-fold increased SNR of the pituitary gland in this model. Lastly, we identify a cadaveric case where transnasal coil 1) identified potential lesion that was not detected on standard head coil and 2) potentially correlated with histologic abnormality. We hypothesize this technique may be applicable to small functioning pituitary tumors.

Increased SNR may be attained by higher field strengths (7T MRI) [8] or a local coil. There is limited published data using this latter strategy. Chittiboina et al. [12], published a cadaveric study using a 12 mm transnasal coil inserted using a microscope-based sublabial approach and imaging performed using a 1.5T scanner. The coil was inserted through the retractor system, and the tip ended up between 4.2 and 17 mm from the pituitary gland. In approximately half of the cases where the coil was in close proximity to the sella there was a mean 10-fold SNR improvement, while the other half of the cases showed an improvement of less than 5-fold. In comparison, our study uses a larger flexible coil placed along the sella through an endonasal endoscopic approach without the need for a custom securing apparatus and with complete visualization both before and after coil placement. The 17-fold SNR improvement would be in some respects equivalent to utilizing a field strength of 51T assuming a linear relation between $B_0$ and SNR [15], which is not practically achievable, and thus shows the ability of a local coil to maximize imaging resolution. Overall, we utilize a similar strategy of image improvement with potentially increased SNR improvements with the more contemporary endonasal endoscopic approach for pituitary surgery.

Of note, the MRI quality in cadaveric tissue is known to be different from clinical images, and therefore the overall image quality is reduced from clinical standards. Despite this known limitation of our study, we demonstrate a difference in SNR between the head coil and transnasal coil, as well as an expected improvement with better spatial resolutions in each coil. In addition, our pathological analysis is limited in that left/right orientation could not be preserved with fixation and staining. Despite this, we found a potential pathological correlate in the pituitary sample with a hypointensity seen on the transnasal coil MRI and may serve as a proof of concept of identification of pituitary lesions not seen on standard MRI.
Overall, these data demonstrate that the flexible transnasal coil can likely be safely used in a clinical setting and has the potential to identify pituitary tumors that are missed on standard clinical MRI sequences. Further research will investigate the safety and feasibility of the transnasal coil in patients undergoing surgery for functional ACTH-producing pituitary tumors with negative imaging.

CONCLUSION

In conclusion, the study describes a transnasally-placed 2 cm flexible coil to improve the resolution of pituitary imaging. The coil is compatible in 95% of patients, can be successfully placed in contact with the sella in cadaver studies, shows no temperature changes in phantom studies during scanning, and improves the SNR of the pituitary by an order of 17. This study provides feasibility data for the promise of application to the clinical setting to improve detection of small ACTH-secreting pituitary tumors when clinical pituitary MRI fails.

Declarations

The authors have no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

Conflict of Interests: None

Funding Support: NREF Clinical Investigator Grant (MB), Jonasson Cancer Center (KP)

ACKNOWLEDGEMENTS

The authors wish to thank individuals who donate their bodies and tissues for the advancement of education and research. The authors would like to express our sincerest gratitude to J. Rock Hadley at the University of Utah, who played a vital role in the initial design and construction of the coil interface with Siemens MRI scanners.

References


Figures
The flexible mini coil design. A 2 cm circular coil apparatus is connected via a 20-cm coaxial cable to a custom circuit box specifically designed for the 3T Siemens scanner at our institution (A). The circuit is also connected with a docking port for connection with the MR scanner (B). The radiofrequency coil was designed with flexibility for transnasal application (C) and a protective coating was applied to the coil to maintain this flexibility (D).
Figure 2

Anatomic measurements of the sphenoid sinus in 50 patients using magnetic resonance imaging T1 with contrast images in the midline sagittal (A) and axial (B) planes. The distributions of the craniocaudal sphenoid distance at various degrees and the lateral intercarotid distance (C). Electromagnetic simulations with a 2 cm radiofrequency coil predicting signal-to-noise ratio increases at various distances from the coil and with various coil rotation angles relative to the horizontal MRI head holder and superposition of these simulations on an MRI T1 with contrast sphenoid sinus region (D).
Figure 3

Meat phantom with direct coil placement and thermometer placement (A) and schematic illustrations of the two temperature measuring sites (B). Temperature recordings at measuring sites S1 and S2 for the 15-minute fast low angle shot three-dimensional imaging (FL3D) sequence scan (C). Cadaveric preparation of the sella with the removal of sphenoid septae and mucosa (D), placement of collagen sponge in clival recess to eliminate air-bone interface artifact (F), placement of flexible mini coil at 0 degrees, and filling of the sphenoid sinus with collagen sponge (G).
Figure 4

Cadaver heads with the placement of the flexible transnasal coil on T1-MPRAGE images with 0.9 mm slice thickness (A), 0.4 mm slice thickness (B), and 0.2mm slice thickness (C). The images were compared with the images from the Siemens 20-channel Head/Neck coil at the same resolutions. The pituitary gland region of interest (marked by white circle) was divided into 4 sub-regions with 3 mm width: Region a, Region b, Region c, and Region d (D). The noise region of interest is identified by the blue circle.
Figure 5

A coronal view of the pituitary gland using high-resolution Proton density (0.2mm x 0.2mm x 0.7mm) image with the transanasal coil in a cadaveric specimen (A) showing highlighted pituitary gland (yellow outline) and hypointensity (red outline). Corresponding coronal sections show a cyst like structure in the lateral aspect of this gland (C,D).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFile.docx