Submission ID #: 61724
Scriptwriter Name: Bridget Colvin
Project Page Link: https://www.jove.com/account/file-uploader?src=18825868

Title: Role of Diffusion MRI Tractography in Endoscopic Endonasal Skull Base Surgery

Authors and Affiliations: Matteo Zoli[1,2]*, Lia Talozzi[2]*, Micaela Mitolo[3], Raffaele Lodi[2,4], Diego Mazzatenta[1,2#], and Caterina Tonon[2,3#]

*These authors contributed equally
#These authors contributed equally

[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Center for the Diagnosis and Treatment of Hypothalamic-Pituitary Diseases - Pituitary Unit
[2]Department of Biomedical and NeuroMotor Sciences, University of Bologna
[3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Functional and Molecular Neuroimaging Unit
[4]IRCCS Istituto delle Scienze Neurologiche di Bologna

Corresponding Author:
Caterina Tonon
caterina.tonon@unibo.it

Co-Authors:
matteo.zoli4@unibo.it
liatalozzi@gmail.com
micaela.mitolo@unibo.it
raffaele.lodi@unibo.it
diego.mazzatenta@unibo.it

Author Questionnaire

1. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or similar? **N**

2. Software: Does the part of your protocol being filmed demonstrate software usage? **Y**

3. Interview statements: Considering the Covid-19-imposed mask-wearing and social distancing recommendations, which interview statement filming option is the most appropriate for your group? **Please select one**.

☒ Interviewees wear masks until the videographer steps away (≥6 ft/2 m) and begins filming. The interviewee then removes the mask for line delivery only. When the shot is acquired, the interviewee puts the mask back on. Statements can be filmed outside if weather permits.

4. Filming location: Will the filming need to take place in multiple locations (greater than walking distance)? **N**

Protocol Length
Number of Shots: **7**

Introduction

1. Introductory Interview Statements

REQUIRED:

1.1. **Raffaele Lodi**: Using an integrated neuroimaging and neurosurgery protocol, it is possible to merge different expertise into a synergic framework to tailor a patient-specific tumor resection surgery **[1]**.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

NOTE: Shot 1.1.1. Take 4 is recommended for use.

REQUIRED:

1.2. **Caterina Tonon**: Using MRI tractography, it is possible to visualize white matter tract dislocation and tumor distances. Its utility in glioma surgery has been established and can also be applied in drug-resistant focal epilepsy **[1]**.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

NOTE: Shot 1.2.1. Take 5 is recommended for use.

OPTIONAL:

1.3. **Diego Mazzatenta**: The integration of advanced neuroimaging techniques in endoscopic endonasal surgery for pituitary-diencephalic and skull base tumors is effective at increasing surgical safety, reducing the complications and improving patient outcomes and quality of life **[1]**.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

NOTE: Shot 1.3.1. Take 8 is recommended for use.

OPTIONAL:

1.4. **Micaela Mitolo**: MRI tractography, combined with task fMRI, allows the monitoring of brain structural and functional reorganization after surgery. In addition, correlations with clinical outcomes are useful for clinical and research purposes [**1**].

1.4.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

NOTE: Shot 1.4.1. Take 4 is recommended for use.

OPTIONAL:

1.5. **Matteo Zoli**: Both endoscopic endonasal surgery and advanced neuroimaging require a long training period. We suggest an observership or a fellowship in academic tertiary referral centers at which these techniques are being implemented **[1]**.

1.5.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera *Videographer: Can cut for time as necessary*

OPTIONAL:

1.6. **Micaela Mitolo**: Through visual demonstration, is possible to standarize the steps of this method and to clarify how to integrate different expertise **[1]**.

1.6.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera *Videographer: Can cut for time as necessary*

Ethics Title Card

1.7. Procedures involving human subjects have been approved by the Comitato Etico Area Vasta Emilia Centro della Regione Emilia Romagna (CE-AVEC).

Protocol

2. Brain Magnetic Resonance Imaging (MRI) Setting and Acquisition Parameters

2.1. Using a standardized multimodal MRI protocol high-field scanner, acquire high-resolution and volumetric anatomical sequences using T1-weighted pre- and post-gadolinium contrast agent administration and FLAIR (flair) T2-weighted imaging **[1-TXT]**.

2.1.1. WIDE: Talent at MRI, acquiring images **TEXT: FLAIR: fluid-attenuated inversion recovery**

2.2. Acquire continuous sagittal slices providing an isotropic resolution of a 1- x 1- x 1-cubic millimeter scanning time of about 5 minutes per sequence **[1]**.

2.2.1. SCREEN: 2.2.1. *Video Editor: can speed up*

2.3. Acquire a high-resolution T2-weighted sequence to localize the tumor area for cranial nerve visualization with a volumetric Constructive Interference in Steady State voxel dimension of 0.5- x 0.5- x 0.5-cubic millimeters and a scanning time of about 9 minutes **[1]**.

2.3.1. SCREEN: 2.3.1. *Video Editor: please emphasize round grey tumor in center of image when mentioned (can speed up)*

2.4. Acquire diffusion-weighted sequences using single-shot echo-planar images, a 2- x 2- x 2-cubic millimeter voxel dimension, 64 magnetic gradient directions with a 2000 second/square-millimeter b-value, 98-millisecond echo time, and 4300-millisecond relaxation time **[1]**.

2.4.1. SCREEN: 2.4.1.

2.5. Acquire five volumes with a null b-value at the beginning of the diffusion-weighted acquisition with the phase encoding direction set to anterior-posterior and a scanning time of 5 minutes **[1]**.

2.5.1. SCREEN: 2.5.1. *Video Editor: can speed up*

2.6. Then acquire three volumes with a null b-value but reversed, posterior-anterior, phase encoding direction to correct any imaging distortions due to the echo planar image acquisition and a scanning time of 42 seconds. Continuous near-axial slices will be acquired **[1]**.

2.6.1. SCREEN: 2.6.1. *Video Editor: can speed up*

3. Tumor Segmentation, Tractography Analysis, and 3D-Rendering Visualization

3.1. For segmentation of the tumor, load the images into the the itk (eye-T-k)-snap software **[1-TXT]** and inspect the tumor in the T1.nii, Flair.nii, and T1_contrast.nii images **[2]**.

3.1.1. WIDE: Talent loading image(s) into software, with monitor visible in frame **TEXT: http://www.itksnap.org**

3.1.2. SCREEN: 3.1.2.

3.2. Then select the anatomical plane to follow when drawing the lesion **[1]**.

3.2.1. SCREEN: 3.2.1. *Video Editor: can speed up*

3.3. For tractographic analysis of the segmented tumor, run the FSL-dtifit (F-S-L-D-T-eye-fit) function to model diffusivity and the different spatial directions and obtain the FA.nii, MD.nii, and V1.nii diffusion tensor maps **[1]**.

3.3.1. SCREEN: 3.3.1: 00:00-00:18 *Video Editor: please speed up*

3.4. Evaluate the diffusion tensor imaging maps to access any abnormal diffusivity values that may occur in the presence of tumor edema or infiltration and select the **seed_image** and **include** options based on a priori anatomical knowledge to adopt a seed-target approach **[1]**.

3.4.1. SCREEN: 3.4.1. *Video Editor: please speed up*

3.5. Then manually draw regions of interest to set the seed or target for tractography **[1-TXT]**.

3.5.1. SCREEN: 3.5.1: 00:13-00:41 *Video Editor: can speed up* **TEXT: Alternative: Use atlas-based ROIs**

3.6. For an accurate description of the diffusion tensor imaging parameters, use along-tract algorithms, such as the Matlab-based algorithm, that model the surface tract geometry with the Laplacian operator properties **[1]**.

3.6.1. SCREEN: 3.6.1. *Video Editor: please speed up*

3.7. To visualize the 3D volume rendering, in the Surf Ice software, click **File** and **Open** in the command panel and select the .obj file **[1-TXT]**.

3.7.1. SCREEN: 3.7.1: 00:00-00:15 *Video Editor: can speed up* **TEXT: https://www.nitrc.org/plugins/mwiki/index.php/surfice:MainPage**

4. Preoperative Clinical Examination and Surgical Planning

4.1. Before scheduling the procedure, perform a neurological physical examination, with a collection of anamnestic information about weight gain, the sensation of hunger, continuous monitoring of the rectal temperature every 2 minutes for 24 hours, and a 24-hour sleep-wake cycle recording **[1]**.

4.1.1. WIDE: Talent evaluating Patient/checking Patient chart or similar

4.2. Based on the results of tumor segmentation and the relationship with the functional eloquent neural structures, discuss the patient candidacy for surgery in a collegial team meeting to determine the most appropriate surgical approach **[1]**.

4.2.1. Talent at table with our Talents, discussing Patient surgical candidacy

4.3. After selecting the surgical corridor with the most minimal risk of injury to the neural structures **[1]**, define the safe resection area for each case, localizing the critical neural structure under which the proximity the resection must be arrested to avoid permanent damage **[2]**.

4.3.1. Talent at computer, selecting corridor with most minimal risk, with monitor visible in frame
4.3.2. SCREEN: 4.3.2.

4.4. Then merge the most relevant MRI sequences **[1]** and import the sequences, including the tractography reconstructions, into the operative phase neuronavigation system **[2]**.
4.4.1. SCREEN: 4.4.1: 00:02-00:10
4.4.2. SCREEN: 4.4.1: 00:12-00:27 *Video Editor: please speed up*
NOTE: Shots 4.4.1. and 4.4.2. were shot by the videographer in one long take.

5. Endoscopic Endonasal Surgery

5.1. Before beginning the procedure, select the brain surgery electromagnetic registration modality **[1]**.

5.1.1. WIDE: Talent selecting modality

5.2. Register the neuronavigation system on the patient, adopting a free-tracking technique or external markers, and control the accuracy of the achieved registration, checking the position of the external markers on the imported MRI **[1-TXT]**.

5.2.1. SCREEN: 5.2.1. *Video Editor: can speed up* **TEXT: Repeat registration as necessary**

5.3. When the patient is ready, use a zero-degree endoscope **[1-TXT]** to harvest the naso-septal flap **[2]**. Next, perform an anterior sphenoidotomy and a posterior septostomy and ethmoidectomy, preserving the middle turbinate as possible **[3]**.

5.3.1. Talent selecting 0° endoscope **TEXT: See text for patient prep details**
5.3.2. LAB MEDIA: surgery: 00:11-00:21
1.1.1. LAB MEDIA: surgery: 00:33-00:56 *Video Editor: please emphasize middle turbinate as possible*

5.4. Open the sellar and tuberculum bones **[1]**. After coagulation of the superior intercavernous sinus, make an H-shaped incision in the dura layer **[2]**. Cleave the tumor by the arachnoidal plane **[3]** and centrally debulk the tumor **[4]**.

5.4.1. LAB MEDIA: surgery: 00:57-01:04
5.4.2. LAB MEDIA: surgery: 01:09-01:29
5.4.3. LAB MEDIA: surgery: 01:50-02:05
5.4.4. LAB MEDIA: surgery: 02:32-03:00

5.5. Remove the tumor capsule from the surrounding diencephalic neural structures **[1-TXT]** and use angled optics to explore the surgical cavity for any remaining pieces of tumor **[2]**. When all of the tumor has been removed, use an intradural intracranial layer of dural substitute to close the osteo-meningeal opening **[3-TXT]**.

5.5.1. LAB MEDIA: surgery: 03:03-03:13 **TEXT: Stop resection if tumor adhered to eloquent structures**
5.5.2. LAB MEDIA: surgery: 03:43-03:52
5.5.3. LAB MEDIA: surgery: 04:31-04:41 **TEXT: Use bipolar coagulation or hemostatic agents to ensure hemostasis**

5.6. Then place an extradural intracranial layer of dural substitute, scaffolded with abdominal fat **[1]** and eventually bone **[2]** and cover the closure with the naso-septal flap **[3]**.

5.6.1. LAB MEDIA: surgery: 04:45-04:50
5.6.2. LAB MEDIA: surgery: 05:07-05:13
5.6.3. LAB MEDIA: surgery: 05:27-05:33

Results

6. Results: Representative Tumor Detection and Endoscopic Endonasal Skull Base Tumor Removal

6.1. In this representative patient **[1]**, brain MRI revealed a suprasellar tumor occupying the opto-chiasmatic cistern and invading the third ventricle with an irregular polycystic morphology **[2]**.

6.1.1. LAB MEDIA: Figure 1

6.1.2. LAB MEDIA: Figure 1 *Video Editor: please emphasize red signal in Figures 1D and 1E*

6.2. The optic pathway tractography **[1]** and bilateral optic cranial nerves were reconstructed **[2]**, but susceptibility artifacts within the interface between the brain, bones, and blood vessels did not allow a complete reconstruction of the fibers connecting the optic chiasm to the optic nerves **[3]**.

6.2.1. LAB MEDIA: Figure 2A

6.2.2. LAB MEDIA: Figures 2A and 2B

6.2.3. LAB MEDIA: Figure 2

6.3. Investigation of the pyramidal tract diffusivity profile and along-tract diffusion tensor imaging map statistics **[1]** showed the presence of a focal FLAIR T2-weighted hyperintensity at the level of the right posterior limb of the internal capsule **[2]**, corresponding to a 5% increase of the right mean diffusivity measure compared to the left side **[3]**.

6.3.1. LAB MEDIA: Figure 3A

6.3.2. LAB MEDIA: Figure 3 *Video Editor: please emphasize Right image in Figure 3C*

6.3.3. LAB MEDIA: Figure 3 *Video Editor: please emphasize red data line in Figure 3B*

6.4. Using an endoscopic endonasal extended transplant-transtuberculum approach **[1]**, the tumor was centrally debulked in conjunction **[2]** with the draining of its cystic component **[3]**.

6.4.1. LAB MEDIA: Figure 4 *Video Editor: please emphasize Figure 4A*

6.4.2. LAB MEDIA: Figure 4 *Video Editor: please emphasize Tumor and Tumor Cyst in Figure 4B*

6.4.3. LAB MEDIA: Figure 4 *Video Editor: please emphasize Cyst Fluid in Figure 4C*

6.5. The craniopharyngioma was then able to be progressively detached from the neural structures to adopt the arachnoid as a cleavage plane **[1]**.

6.5.1. LAB MEDIA: Figure 5 *Video Editor: please sequentially add/emphasize Figures 5A-5D*

6.6. At the end of the surgery, complete tumor removal with preservation of the hypothalamic anatomy was achieved **[1]**.

6.6.1. LAB MEDIA: Figure 6 *Video Editor: please sequentially add/emphasize Figure 6A-6C*

6.7. The repair of the osteo-dural defect was then performed **[1]** using abdominal fat **[2]** and the naso-septal flap **[3]**.

6.7.1. LAB MEDIA: Figure 7
6.7.2. LAB MEDIA: Figure 7 *Video Editor: please emphasize Fat in Figure 7B*
6.7.3. LAB MEDIA: Figure 7 *Video Editor: please emphasize Naso-septal Flap in Figure 7D*

6.8. Three months after the surgery, a complete tumor removal, with no remnant or recurrence, was observed **[1]**.

6.8.1. LAB MEDIA: Figure 8 *Video Editor: please emphasize Figure 8B*

Conclusion

7. Conclusion Interview Statements

7.1. **Diego Mazzatenta**: In the pre-operative workup, the most relevant steps are an accurate diffusion-weighted sequences acquisition and tumor segmentation. During surgery, the key point is an accurate identification of the neural structures **1]**.

INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera (3.1., 5.6.)

NOTE: Shot 7.1.1. Take 1 (second part)is recommended for use.

7.2. **Diego Mazzatenta**: The visualization of neural structures, provided by this method, can be adopted for all skull base regions, reducing the risk of permanent disabilities for many other tumors **[1]**.

7.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

7.3. **Raffaele Lodi**: The tractographic reconstruction of cranial nerves and neural pathways can facilitate our understanding of the relationship between tumors and these structures, potentially providing an innovative outcome predictor for patient symptoms **[1]**.

7.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera *Videographer: Can cut for time as necessary*

NOTE: Shot 7.3.1. Take 4 is recommended for use.