Implementation of a Process for Radiosurgery Incorporating Functional Magnetic Resonance Imaging

Ricardo Ruggeri, MSc.[1]; Elira Lomban, M.D.[2]; Belen Ibañez, M.D.[3]; Marcelo Paolini[4]; Silvia Hansing, M.D.[5]

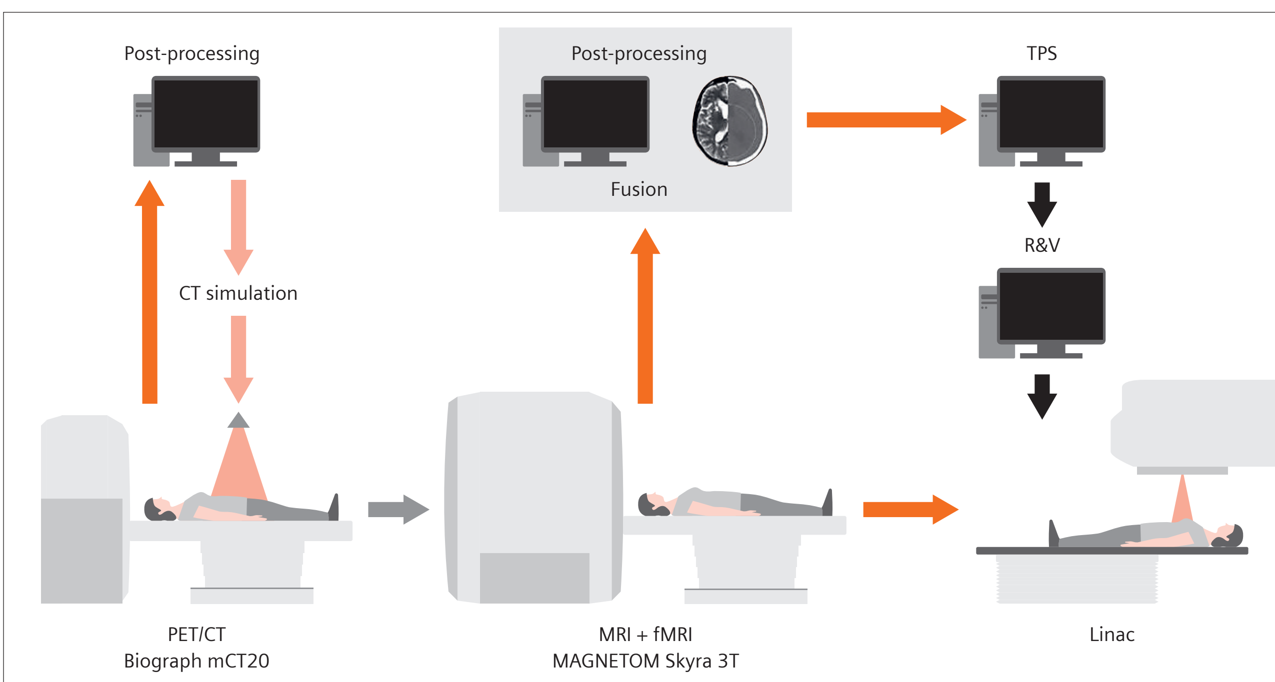
[1]Medical physics department, Leben Salud, Patagonia, Argentina
[2]Nuclear magnetic resonance department, Leben Salud, Patagonia, Argentina
[3]Neuroradiology department, Leben Salud, Patagonia, Argentina
[4]Multimodal images post-processing department, Leben Salud, Patagonia, Argentina
[5]Radiotherapy department, Leben Salud, Patagonia, Argentina

Introduction

The history of radiosurgery as an option for radiotherapy treatment has its origins in the 1950s, in the work of a Swedish team led by neurosurgeon Lars Leksell. The technique was defined as "the destruction of an intracerebral target, localized stereotactically, without craniotomy, in a single fraction of ionizing radiation, delivered through a system of convergent beams in the target".

Technological advances for radiosurgery in linear accelerators were led by Derechinsky and Betti in Buenos Aires, Argentina. In 1982, they developed and adapted the non-coplanar beams technique using this equipment. In the same period, major advances in computation and in CT and MR imaging occurred, which triggered an explosion in the development and use of radiosurgery, improving and assuring the localization of small lesions and simplifying management.

The incorporation of six-degrees-of-freedom robotic couches, multileaf collimators (MLC), and tridimensional imaging systems like cone beam CT in modern linear accelerators created a need for high-quality medical images that would improve the delineation of the target and organs at risk (OARs).



1 The SRS process at COI, integrating fMRI.

Multimodality imaging has been enormously relevant in cutting-edge radiosurgery procedures. Magnetic resonance imaging (MRI) has prevailed over other modalities for its ability to incorporate different acquisition sequences into the same exam. This allows the use of functional magnetic resonance imaging (fMRI), which can be used by radiotherapists to determine dose prescription, and by medical physicists to optimize treatment in the treatment planning system (TPS).

These developments are the result of a clear need not just to preserve the maximum amount of healthy brain parenchyma, but also to know the exact location of eloquent areas related to motor, visual, language, and memory functions. These areas can then be taken into account during treatment planning and patient follow-up.

Enabling our patients to remain active in society, with minimum impact to their quality of life, was our motivation to include cerebral fMRI in our radiotherapy planning protocol.

In the following article, we discuss the benefits of performing fMRI when planning stereotactic radiosurgery (SRS) in patients with primary or secondary brain tumors. We also provide the necessary information regarding implementation protocols.

Problems and challenges

Initially, MRI was used to identify small lesions and to accurately segment these lesions and the surrounding OARs. However, incorporating MRI raised new technical issues that should be taken into account, such as:

- geometrical distortion of the image due to the equipment's characteristic gradients;
- the use of MRI-compatible immobilization devices;
- incorporation of post-processing software that works with multimodality images (CT, PET, etc.), and its corresponding registration and deformable fusion;
- coil configuration for adaptation to SRS immobilization devices;
- sequence and/or acquisition protocol design to achieve a 3D isotropic reconstruction with high resolution and high signal-to-noise ratio.

There are also a number of common obstacles, such as access to an MRI scanner. Indeed, few radiotherapy institutions possess exclusively or even partially dedicated MRI scanners.

Another aspect to consider is the training of MRI technologists, who must understand the image-quality requirements for radiosurgery and how to handle patients when using immobilization devices.

Finally, the issue of reimbursement of MRI must also be considered, as this is an essential factor in deciding whether to use this particular treatment technique.

Technology and general workflow

The radiosurgery process at Centro Oncológico Integral (COI) starts with the patient's CT simulation using a Biograph mCT 20 PET/CT scanner. A CT or PET/CT scan is performed according to the radiotherapist's request, and single or multiple treatment isocenters are located with five mobile lasers, which move in the three Cartesian axes. The CT images and the isocenter location(s) are stored in the *syngo*.via RT Image Suite (RTiS) workflow.

Afterwards, the patient is scanned with the 3T MRI scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany). The specific acquisition sequences include fMRI for accurate structure contouring and delineation of eloquent areas or regions.

During post-processing, bioimaging graduates register multimodality images, segment OARs, and obtain fMRI results using *syngo*.via post-processing workflows. The radiotherapists then contour the lesions with their respective margins – gross tumor volume (GTV), clinical target volume (CTV), and planning target volume (PTV) – and decide on the best therapeutic strategy.

All the information is consolidated in the *syngo*.via RTiS workflow and exported to the TPS, where medical physicists perform planning and validation using a patient-specific QA. Once all verifications and relevant controls have been carried out, patient irradiation in the linear accelerator occurs.

The process requires uniform positioning criteria, MRI-compatible immobilization devices, and the availability of flat indexed couches. It also demands connectivity between acquisition software, image post-processing software, treatment planning system, and the record-and-verify system.

Connectivity with the radiosurgery TPS is crucial, especially when image sequences and contoured structures are exported from the post-processing system.

In what follows, we will describe the subprocess of fMRI for SRS, including the acquisition of the fMRI sequence, the results, and their use in the RT workflow with *syngo*.via RTiS.

Physical principles of fMRI

fMRI can help to preserve eloquent areas by locating visual, motor, and language functions. This is done by using specific paradigms for each function and the blood-oxygen-level-dependent (BOLD) technique.

BOLD signal obtained in fMRI uses the endogenous paramagnetic contrast agent, deoxyhemoglobin.

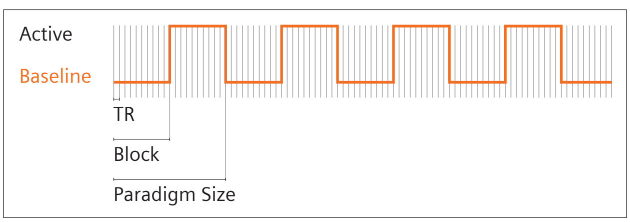
Motor, verbal, or visual stimulation paradigms activate the motor cortex, which increases cerebral blood flow and local oxygen consumption. This causes a rise in deoxyhemoglobin concentration in the capillary veins, which leads to a T2* signal loss caused by magnetic susceptibility.

Gradient-echo sequences are most sensitive to the magnetic susceptibility phenomenon. They are typically echo-planar-imaging (EPI) sequences that allow whole-brain coverage with good temporal resolution and minimal risk of motion artifacts.

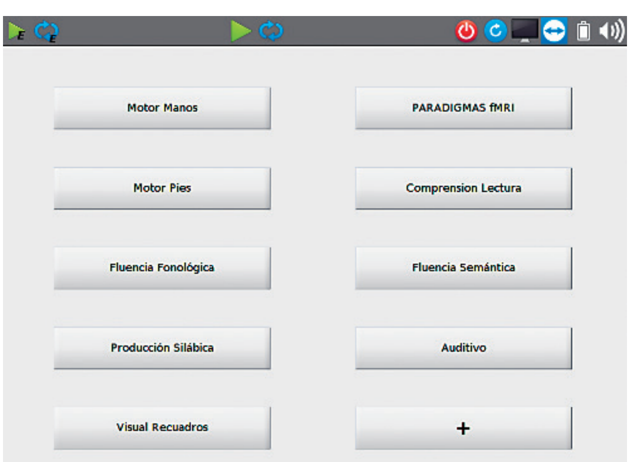
The fMRI examination includes a stimulation paradigm for each cerebral area of interest. The most frequently used paradigms are motor, verbal, and/or visual.

Each of these paradigms involves a task that must be explained thoroughly to the patient, who then practices it before the acquisition.

During the examination, stimulus periods of 30 seconds are alternated with 30 seconds of rest. This is repeated for a maximum of seven minutes, and constitutes a paradigm.



2 Schematic representation of a block design: The orange curve represents active blocks (Task ON) and baseline blocks (Task OFF). The points between the vertical lines represent measurements of cerebral volumes, which take some time to acquire. Here we can see ten measurements per block, with a total of 90 measurements. The size of the paradigm is a vectorial parameter in the BOLD sequence chart, which represents the state OFF+ON. In this example, the size of the paradigm would have ten baseline measurements and ten active measurements (= 20). *Reproduced with permission from MAGNETOM Flash (75) 4/2019 How-I-do-it, Clinical fMRI: Where do I start? Victoria Sherwood and Tina Pavlin, NordicNeuroLab AS, Bergen, Norway.*



3 Paradigm menu, for study and training.

Exam preparation

Prior to entering the scanner room, the patient spends roughly 15 minutes practicing each of the paradigms to be executed during the exam. This is to ensure that they understand the task so the exam will succeed.

The paradigm must be programmed (Fig. 3) to show the right activity at the moment of the stimulus, according to which part of the brain is to be stimulated: moving the hands and feet for the motor paradigm (this can include opening or closing the fists, flexing and extending the toes, or pressing the thumb against each finger in an exaggerated manner); choosing the correct verb or adjective in a simple sentence for the verbal paradigm; and being exposed to flash-like visual stimuli with a black-and-white grid for the visual paradigm.

Exam protocol

The protocol includes three essential sequences that must be executed at the beginning of the exam to enable correct post-processing:

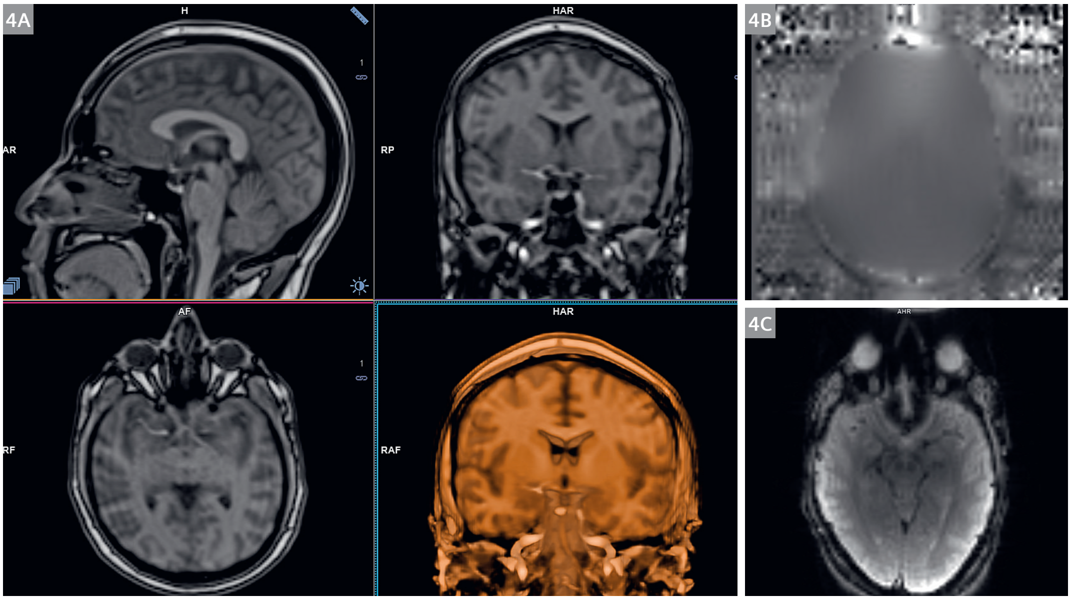
- ANATOMY t1_mprage_sag_p2_iso
- FIELD MAP gre_field_mapping.
- BOLD ACTIVATIONS ep2d_bold_moco_p2_s2

The paradigms are executed in approximately 30 minutes. The t1_mprage_sag_p2_iso sequence is acquired as an anatomical map that will demonstrate the corresponding activations; a 3D FLAIR isotropic sequence can also be used for the same purpose. The field map (GRE field mapping) contains data for motion correction (MOCO, **Mo**tion**Co**rrection). BOLD activation sequences demonstrate the corresponding function for each paradigm (Fig. 4). BOLD sequences are adapted according to the paradigm. This affects the number of measurements (Fig. 2), which translates into either an increase or decrease in acquisition time.

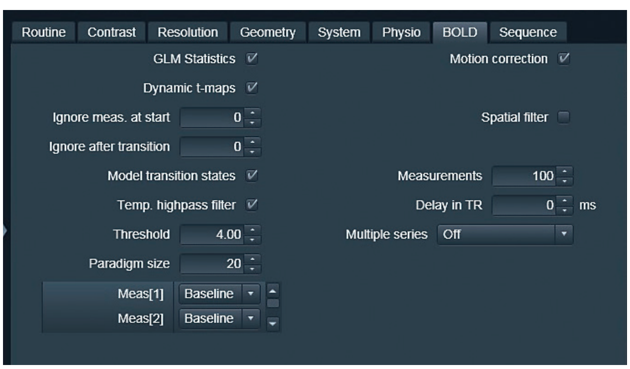
Acquisition

After the patient has practiced the paradigms, they are positioned in the MRI scanner in a room containing all the necessary equipment. The exam can then begin. We use a 32-channel head coil, shown in Figure 6A, which delivers images with a higher signal-to-noise ratio. The coil is fitted with a mirror (orange arrow) that displays the different paradigms to the patient. Figure 6B shows the MAGNETOM Skyra workstation with software version *syngo*.MR E11.

The paradigms are displayed to the patient on the screen (retro projection). Figures 7A and 7B show the verbal and motor paradigms, respectively. After acquisition of localizer, anatomy, and field map sequences (Fig. 4), the generation of specific BOLD sequence paradigms begins (Fig. 7).



4 Anatomy **(4A)**, field map **(4B)**, and BOLD sequences **(4C)**.

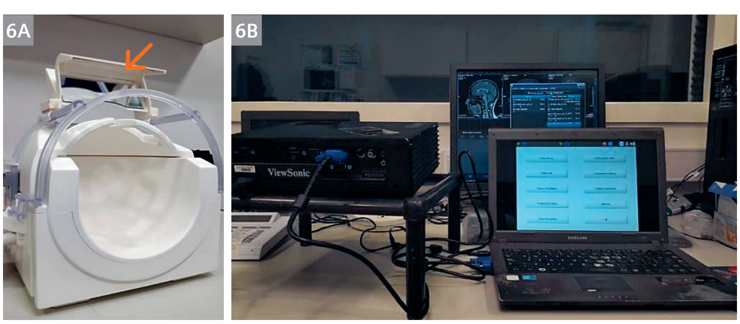


5 BOLD sequence configuration with 100 measurements, a paradigm size of 20, and motion correction.

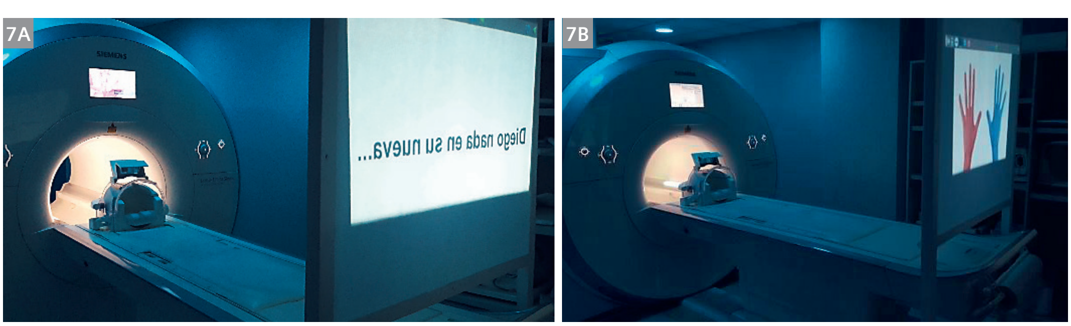
Sequences and acquisition times

Sequence	Voxel size	Number of slices	FoV	Acquisition time
T1 MPRAGE AXIAL	0.9 x 0.9 x 0.9 mm	176	240	5:00 min.
GRE FIELD MAPPING	3.4 x 3.4 x 3.0 mm	36	220	0.54 min.
BOLD ep2d	2.3 x 2.3 x 3.0 mm	52	220	7:00 min.

Table 1: Essential sequences for an fMRI exam using a MAGNETOM Skyra 3T scanner.



6 **(6A)** The 32-channel head coil with mirror (orange arrow) for displaying the projected image inside the room. **(6B)** MAGNETOM Skyra workstation, projector, and laptop for activating the corresponding paradigms.



7 Verbal paradigm **(7A)** and motor paradigm **(7B)**.

syngo.MR Neuro 3D workflow post-processing

After finishing the MRI exam with the paradigms corresponding to the areas of interest, image post-processing begins. This involves loading the images into *syngo*.via (software version VB30) and using *syngo*.MR Neuro 3D (Fig. 8).

The paradigms requiring assessment are then selected – for example, the visual paradigm (Fig. 9).

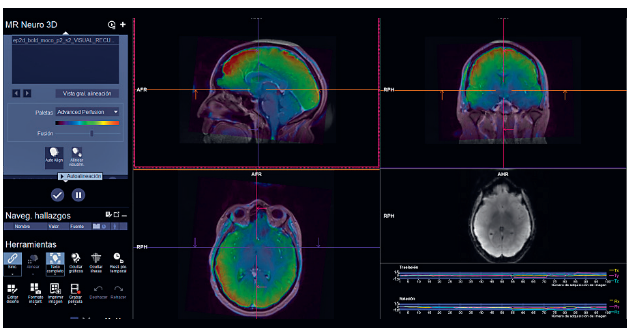
Activations can be visually evaluated and quantified using the volume of interest (VOI) measurement as seen in the example in Figure 10.

The curve obtained shows consecutive stages of activation and rest during the paradigm.

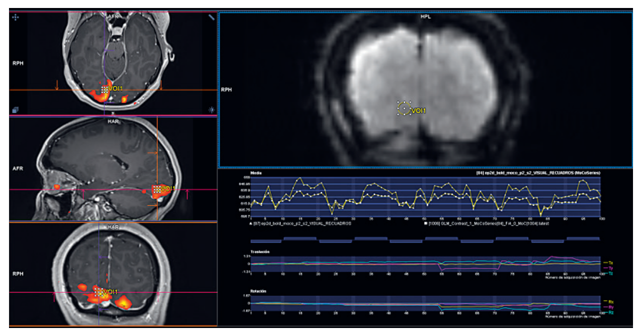
The paradigms cause brain activations in the association, coordination, and motion-initiation areas. Activations in satellite areas that do not match the study's paradigm also occur. These can be differentiated from activations of interest by assessing the activation-rest curve with adapted VOI (Fig. 11).

Figure 11 shows an area of brain parenchyma where VOI does not indicate activation for the studied paradigm.

Next, two examples (Figure 12) of activations that are useful for contouring eloquent areas.

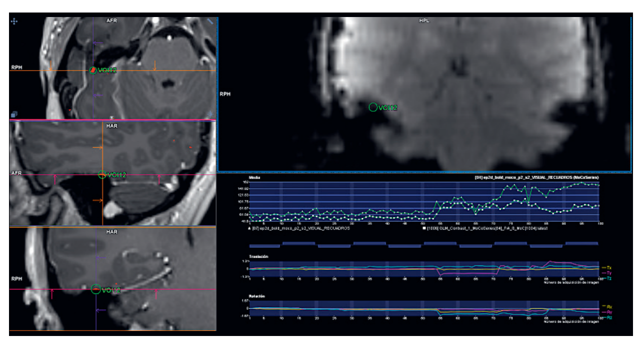


8 *syngo*.MR Neuro 3D with the visual paradigm loaded.

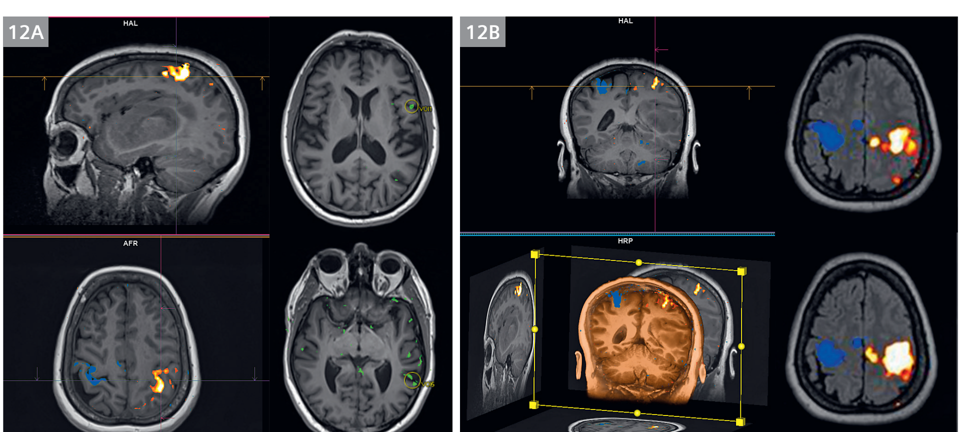


10 VOI measurement for the visual paradigm (VOI used for dynamic evaluation).

9 Sequence selection for post-processing.



11 VOI showing an uptake area not related to the activation paradigm studied.



12 **(12A)** Pulmonary secondary tumor; verbal paradigm involving reading comprehension, identifying Broca and Wernicke's areas in the left hemisphere, dominant; **(12B)** Glioma patient, tumor not seen in this slice; motor paradigm activation of both hands; BOLD signal in primary motor areas obtained bilaterally; the activation area of the left hand is represented in blue, and the right hand in yellow.

syngo.via RT Image Suite workflow

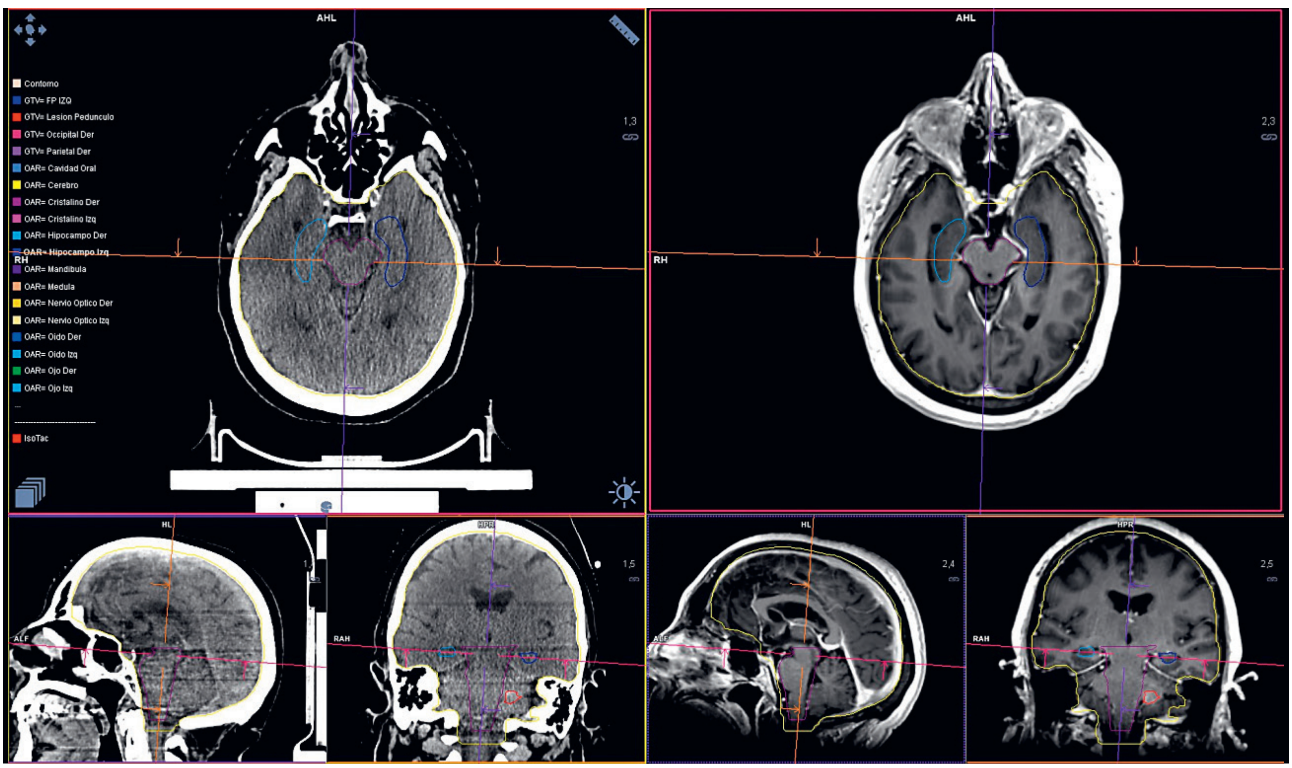
Once the images with the activated areas have been obtained, they are transferred in DICOM RGB format from *syngo*.MR Neuro 3D to *syngo*.via RTiS and registered with the patient's CT images acquired during CT simulation. The activated areas can be then contoured and the contours are automatically shown in the planning CT images. After that, the target volume and tumors are also delineated.

In this part of the process, the T1 MPRAGE sequence is fused with CT images and delineates OARs, such as the hippocampus (Fig. 13). Reconstruction (VRT) is also performed for assessment, as shown in Figure 14.

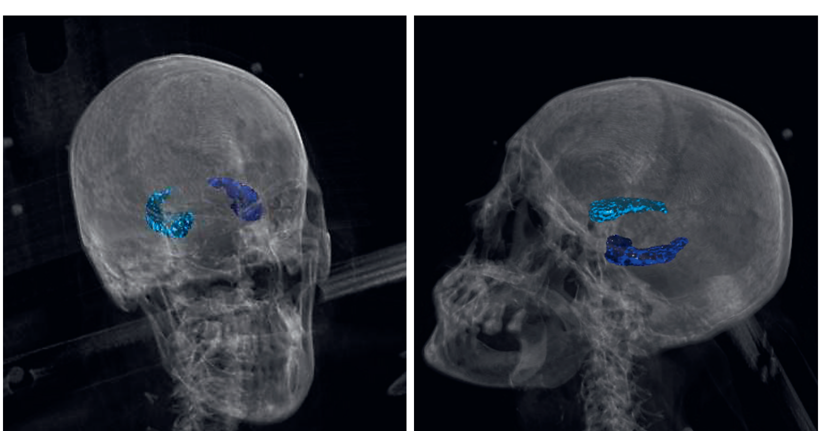
Discussion

For years, radiation oncologists have thoroughly contoured tumors on images, while understanding that OAR contouring is also important for successful treatment. Healthy organs limit the final prescription dose, which is linked to the patient's quality of life.

Progress in the area of MRI has improved the definition and categorization of structures, which has provided the high level of therapeutic certainty required for ablative radiotherapy treatments such as stereotactic radiosurgery (SRS). Nowadays, the ability to explore functional areas of the brain using fMRI is creating great interest for integrat-



13 *syngo*.via RTiS workflow: the CT images from CT simulation are on the left; the MR T1 MPRAGE images obtained in axial orientation, including the hippocampus registration and delineation, are on the right.



14 Transparent VRT visualization to assess OARs.

ing this type of diagnostic study into precision treatments such as radiosurgery – always with the key objective of improving the patient's quality of life.

By incorporating fMRI into the patient's entire diagnostic and treatment process, medical physicists have more information for radiosurgery and conventional radiotherapy treatment planning. Here at COI, we have been able to perform multimodality image fusion, contour eloquent regions in *syngo*.via RTiS, and export them to the treatment planning system.

It is expected that multimodality contouring platforms will eventually incorporate MRI and other modalities besides CT imaging, with compatible segmentation. Unfortunately, fMRI is rarely used to segment eloquent areas for SRS. This means no applications exist that bring together fMRI reconstruction tools with structure segmentation tools such as *syngo*.via RTiS.

In addition, few centers around the world have the equipment and organizational capacity needed to integrate fMRI into SRS, which is one reason why no relevant protocols exist and why very little work has been done on this topic.

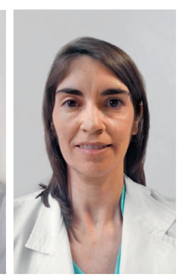
Integrating fMRI into the radiosurgery process has been a great challenge for our radiotherapy and MRI services. Efforts have mainly focused on saving time and associated costs because fMRI has low reimbursement, being a novel technique in the region. Despite the obstacles described, the high level of interest that professionals and Leben Salud's directors have expressed for seeing results and conclusions in this area in the future was the main incentive for incorporating it into standard procedures at our institution.

Contact

Ricardo Ruggeri, MSc.
Technical director and
head of medical physics department
Centro de Oncológico Integral (COI),
a member of the Leben Salud group
Industriales Neuquinos 2800
Neuquén, Patagonia
Argentina
rruggeri@lebensalud.com
Follow me on LinkedIn:
https://www.linkedin.com/in/ricardoruggeri/


Ricardo Ruggeri


Elira Lomban

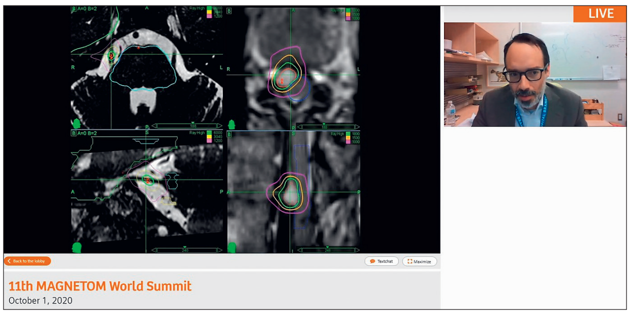

Belen Ibañez


Marcelo Paolini


Silvia Hansing

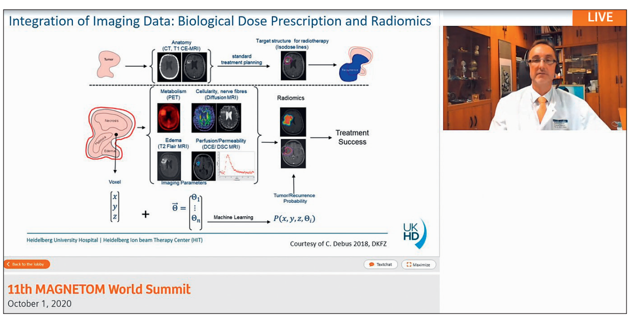
The Integration of MRI in Radiation Therapy:

The Power of Multidisciplinary Collaboration



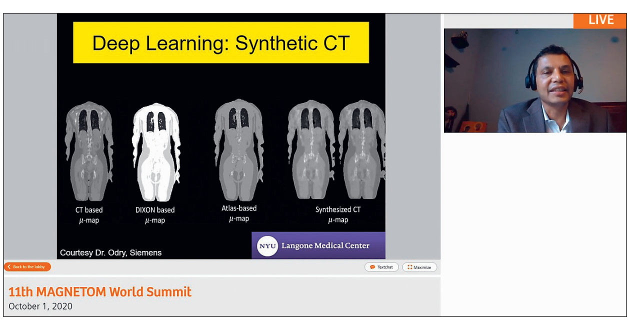
Implementing a Magnet Dedicated to Planning Radiotherapy Treatments

David Roberge
Centre Hospitalier de l'Université de Montréal, Canada



MRI in Radiation Oncology. See what you treat – treat what you see

Juergen Debus
University Hospital Heidelberg, Germany



Collaboration between Radiology and Radiation Oncology for MR-guided Radiotherapy

Hersh Chandarana
NYU, New York, NY, USA

Don't miss the talks delivered by experienced and renowned experts at the MAGNETOM World Summit

www.siemens-healthineers.com/MWS2020-recordings