Integration of Functional Magnetic Resonance Imaging and Magnetoencephalography Functional Maps Into a CyberKnife Planning System: Feasibility Study for Motor Activity Localization and Dose Planning

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OBJECTIVE: **Magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) provide noninvasive localization of eloquent brain areas for presurgical planning. The aim of this study is the integration of MEG and fMRI maps into a CyberKnife (CK) system to optimize dose planning.**

METHODS: **Four patients with brain metastases in the motor area underwent functional imaging study of the hand motor cortex before radiosurgery. MEG data were acquired during a visually cued hand motor task. Motor activations were identified also using an fMRI block-designed paradigm. MEG and fMRI maps were then integrated into a CK system and contoured as organs at risk for treatment planning optimization.**

RESULTS: **The integration of fMRI data into the CK system was achieved for all patients by means of a standardized protocol. We also implemented an ad hoc pipeline to convert the MEG signal into a DICOM standard, to make sure that it was readable by our CK treatment planning system. Inclusion of the activation areas into the optimization plan allowed the creation of treatment plans that reduced the irradiation of the motor cortex yet not affecting the brain peripheral dose.**

CONCLUSIONS: **The availability of advanced neuroimaging techniques is playing an increasingly important role in radiosurgical planning strategy. We successfully imported MEG and fMRI activations into a CK system. This additional information can improve dose sparing of eloquent areas, allowing a more comprehensive investigation of the related dose-volume constraints that in theory could translate into a gain in tumor local control, and a reduction of neurological complications.**

INTRODUCTION

In recent years the fusion of computed tomography and magnetic resonance imaging (MRI) has become a standard aspect of planning of radiotherapy and radiosurgical treatments. The merged images provide optimal morphologic information about the target and the organs at risk. More recently, in selected cases, the need of a better target definition has led to the integration of computed tomography and positron emission tomography, as well as 3-dimensional angiography images, in most treatment planning systems (TPSs).[1] At the same time to obtain functional information about the brain areas, dedicated tools to import and include functional magnetic resonance imaging (fMRI) results in many TPSs have also been developed.[2] Such functional information is useful to identify particular regions of the brain (e.g., the motor or language areas) that would cause significant patient morbidity if compromised.

Key words
- CyberKnife
- Eloquent area
- fMRI
- Integration
- MEG
- Neuroimaging
- Radiosurgery

Abbreviations and Acronyms
BOLD: Blood oxygen level dependent
CK: CyberKnife
EMG: Electromyography
fMRI: Functional magnetic resonance imaging
MEG: Magnetoencephalography
MRF: Movement-related field
MRI: Magnetic resonance imaging
PTV: Planning target volume
TPS: Treatment planning system

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Accurate pretreatment brain mapping may become crucial in cases of functional treatments (i.e., epilepsy, arteriovenous malformation) or when a patient undergoes a treatment for a tumor located proximal to eloquent brain regions. At our institution, various advanced imaging techniques for functional brain mapping and for the diagnosis and clinical management of brain diseases is available, among which are fMRI and magnetoencephalography (MEG).

Functional MRI uses the blood oxygen level dependent (BOLD) signal contrast as a surrogate marker of neuronal activity and depends on the local vascular geometry and physiology.[3] Because of its noninvasiveness and widespread availability, fMRI has gained acceptance during the past 2 decades as an important tool for presurgical and radiosurgical planning.[4] This technique is characterized by high spatial resolution and low temporal resolution, compared with MEG, because the BOLD signal is an indirect measurement of neuronal activity by the assumption of a hemodynamic correlation.

MEG noninvasively measures the magnetic fields generated by neuronal activity of the brain. In particular, magnetic source imaging produces functional maps of brain activity with high temporal resolution, used mainly for the localization of epileptogenic zones and presurgical mapping of eloquent areas.[5] MEG can be particularly valuable to identify functional areas to aid in the radiosurgical treatment of arteriovenous malformations, where the vascularization is disrupted and the BOLD effect might produce altered activations.

Several published studies[6] suggest that MEG and fMRI activations are mostly congruent and consistent with intraoperative localization. However, discrepancies have also been reported in some cases,[7] and the 2 techniques play a complementary role in presurgical mapping.[8-10]

Only a limited number of articles have been published reporting the state-of-the-art neuroimaging integration into a radiosurgery TPS.[11] For example, recent studies by Bowden et al[12] and Conti et al[13] aimed to integrate multimodal data in radiotherapy. To our knowledge, MEG and fMRI have never been jointly implemented in a CyberKnife (CK) system. Bearing this in mind, in the present study reports on our experience in developing a method of integrating MEG and fMRI maps to guide the dose planning strategy in the treatment of brain tumors.

METHODS

This theoretical investigational study defines the possibility of integrating the MEG data into the CK TPS. Treatment data are reported only with the intent of defining the entity of the dose distribution variation according to the different treatment optimizations. The patients were treated according to our institutional clinical practice, not taking into account the information obtained by the functional findings. Because of the lack of comparative data and the pure theoretical design of the study, no conclusions about clinical impact of the treatment should be deduced.

Subjects

Four patients (2 women and 2 men; mean age, 59.5 years; range, 44–68 years) presenting with a solitary brain metastasis from solid tumors were enrolled between December 2013 and November 2015. Tumors were all located in close proximity to the right-hand motor cortex and had a mean volume of 8.28 cm^3 (range, 1.1–21.2 cm^3). At the treatment time 2 patients were free from neurological deficits (patients A and B), whereas the other 2 (patients C and D) showed a mild hemiparesis.

All patients were able to perform the specific task used to produce fMRI and MEG functional maps of the motor-related brain activation. To avoid possible distortions of the weak magnetic field generated by neuronal activity, MEG data collection was always performed before fMRI acquisition.

MEG

Experimental Protocol. During the visually cued motor tasks, subjects were instructed to perform a brisk extension of the affected hand when a cue was presented on a monitor located in front of them. Subjects were instructed to keep their head as still as possible throughout the experiment, to keep their eyes open, and to avoid blinking during the movement execution. Each subject was trained for several minutes before the experiment. The movement was monitored by electromyography (EMG) and visual observation. At least 100 movements were recorded for the subsequent analysis.

Data Acquisition. MEG data were acquired using a 306-channel whole head neuromagnetometer (Triux, Elekta Oy, Helsinki, Finland). In addition, electrooculograms and electrocardiograms were acquired and used for artifact removal. EMG activity was recorded with pairs of Ag/AgCl surface electrodes placed bilaterally on the index and carp flexor muscles.

To estimate the head position in the MEG helmet during the acquisition, 3 anatomic landmarks (left/right auricular, nasion), 600–800 points on the patient's scalp, and the head position indicator coils localization were digitized before signal registration using a 3-dimensional digitizer (Fastrak, Polhemus, Colchester, Vermont, USA). The head position indicator coils remained activated during the recordings monitoring head movements. All the data were recorded at the rate of 1 KHz.

MEG Analysis. MEG data were preprocessed off-line using the spatiotemporal signal-space-separation method to subtract any interference and correct for head movements.[14] MEG data were then band-passed filtered at 0.1–100 Hz. Movement onset was determined by the beginning of the burst of EMG activity. The data were therefore segmented in epochs from 1 second before to 1 second after the movement onset. Epochs with amplitude exceeding 3×10^{-10} T/cm (gradiometers), 3×10^{-10} T (magnetometers), or 150 μV (electrooculogram) were discarded, which resulted in at least 40 artifact-free epochs that were used to calculate average event-related fields for each subject. Movement-related field (MRF) component was identified as peaking 30–40 milliseconds before movement onset.[15] A boundary element model was used to compute the forward model created for each participant by using Freesurfer software package (Martinos Center for Medical Imaging, Charlestown, Massachusetts, USA). To determine the spatiotemporal distribution of cortical sources associated with MRF, a volumetric distributed source modeling using the dSPM[16] method was used. The source distribution at