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RESEARCH

Integrating Functional MRI Information into Radiotherapy Planning of CNS Tumors-Early Experiences

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Abstract The purpose of our study was to examine the integration of functional MRI (fMRI) information into 3D based planning process of the central nervous system (CNS) malignancies. Between 01.01.2008 and 01.12.2008 four patients with astrocytoma were enrolled to this study. Before the planning process conventional planning CT, postoperative MR and individual functional MRI examinations were delivered. For the functional MRI examination the following four types of stimulus were applied: acoustic, visual, somatosensory and numeral. Three different theoretical planning situations were applied and compared: 3D conformal plan without fMRI information, 3D conformal plan with fMRI information and IMRT plan with fMRI information. For plan comparison DVH analysis, and NTCP model were used. fMRI based OR definition resulted in 4 additional OR's in the contouring process. As these cases demonstrate, an average of 50% dose reduction was achieved in OR, OR2 and OR3 with IMRT and fMRI based 3D planning, especially in case of midline localization and big tumor extent. IMRT provides additional sparing effect in the optic tract and brainstem, especially for localizations close to the midline. Our results demonstrated that using fMRI information in conventional 3D based treatment planning potentially benefits significant dose reduction in critical organs, with no compromise in PTV coverage. fMRI can be widely used even in low grade cases (long life expectancies, lower acute and late toxicity in radiotherapy) and in cases with high grade astrocytomas or metastases (higher dose to PTV with better risk organ sparing in radiotherapy).

Keywords CNS tumor · fMRI · Radiotherapy

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Background and Purpose

Astrocytomas are the most common primary Central Nervous System (CNS) tumors. High grade astrocytomas (HGA) occur more frequently compared to the low grade type; the incidence of these tumors is increasing [9]. 3D based conformal radiotherapy is considered as the standard therapy for patients both with low and high-grade HGA following either maximal excision or biopsy [15, 18]. In case of low grade gliomas surgery is the first treatment of choice, but the role of 3D radiotherapy—in postoperative (residual tumor) or definitive (contraindication of surgery) cases—is unquestionable. Currently, various irradiation techniques are used (from brachytherapy to IMRT-intesity modulated radiotherapy) in the modern radiotherapy of astrocytomas. The increase of the maximum dose in 3D based radiotherapy of high grade astrocytomas has led to higher survival rates [16]. Further dose escalation is strongly limited by the tolerance of critical structures. Acute and late side effects could result in serious neurological and hormonal dysfunctions.

In the case of high grade astrocytomas, radiation dose increase is of high importance. The local control rate and survival rate for HGA's show improvement when the radiation dose is escalated from 40 to 60 Gy [3]. The dose of 60 Gy often does not guarantee local control, therefore, there is a general interest in employing higher radiation doses for HGA due to the benefit observed in other locations [3, 4] even if the dose-response curve beyond 60 Gy is lacking.

Functional magnetic resonance imaging (fMRI) is an imaging technique that predominantly uses a gradient echo EPI (Echo Planar Imaging) sequence to define the locations of eloquent cortices, such as the motor cortex, Broca's area, Wernicke's area, visual cortex, etc., in the brain [13, 14]. Integrating fMRI information into the radiotherapy planning process can potentially allow for the delivery of adequate RT (radiotherapy) dose to the target while limiting the dose to the adjacent functional cortex [4].

Our purpose was to present our initial experiences of incorporating fMRI-based information into the 3D treatment planning process. We used our planning software fusion tool to register the acquired fMRI data with the diagnostic MRI and planning CT data. In this study we analyzed different planning situations and techniques to study the impact of fMRI data integration on treatment plans.

Method

Patients

Between 01.01.2008 and 01.12.2008 four patients with astrocytoma were enrolled to this study. Following detailed explanation of the nature of the procedure, all patients provided written informed consent under an institutionally approved subjects research protocol. This study was performed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975 and 1983. Patient characteristics shown on Table 1.

Planning Process

For the patient immobilization an individual thermoplastic mask fixation unit was used (ORFIT) with a standard head mask. After preparation, masking and simulation, the planning CT was performed using a Siemens Somaton Sensation 16 multislice CT unit (continuous slice thickness of 4 mm with 1 mm interspacing, range: from 1 cm above the cranium to Th-6). According to the Diagnostic Department's protocol, a postoperative whole-brain MRI examination was performed (FLAIR, MPR, T1, T2 and post contrast T1 weighted, 4-mm slice thickness, zero spacing in the axial, coronal, and sagittal planes). The CT and MRI acquisition data were sent to the planning system (CMS-XIO version: 4.34.02) in DICOM format.

fMRI Image Acquisition

1.5 T Siemens Magnetom Avanto scanner was used for the functional MRI examinations. Initially, structural scans were acquired for the localization of activation. An axial T1-weighted MP-RAGE sequence (TR: 1160 ms, TE: 4.3 ms, slice thickness: 0.8 mm, number of slices: 192, FA: 15°, matrix: 512*432, field of view: 170*210 mm) were obtained using an 8 channel head coil. BOLD fMRI scans were acquired using an EPI (echo planar imaging) sequence in the same position as the structural images with the following scanning parameters: TR: 3140 ms, TE: 50 ms, slice thickness: 4 mm, number of slices: 170*30, FA: 60°, matrix: 64*64).

Experimental Paradigms

The following four types of stimulus were applied: acoustic, visual, somatosensory and numeral. The measurement sequence of all four paradigms consisted of a 31.4 second activation period (10 scans) followed by a 31.4 second rest period (10 scans), repeated 8 times. The measurements always began with an initial rest period.

In the first paradigm the patients were asked to lie still and listen to a Hungarian and English text (4-4 alternately).

In the second paradigm, a somatosensory stimulus was applied to the patient's hand between thumb and forefinger with difference force (4 soft and 4 strong alternately).

In the third paradigm, a visual stimulus was applied, a check board was projected into the patients field of view.

Table 1 Patient characteristics

	Age	Gender	Primer tumor localization- size	Perifocal oedema	Surgery	Hystology	Dose
Patient 1	38	female	central, 33×25×29 mm	yes	biopsy	Low Grade Asrtocytoma (WHO Grade II)	40+20 Gy
Patient 2	31	male	central, 64×111×70 mm	yes	biopsy	Low Grade astrocytoma (WHO Grade II)	40+20 Gy
Pateint 3	58	female	left parietal, 49×30×20 mm	yes	Incomplete surgical resection	High grade astrocytoma (WHO Grade III–IV)	40+20 Gy
Patient 4	32	female	left occipital, 42×28×39 mm	yes	Incomplete surgical resection	Low Grade astrocytoma (WHO Grade II)	40+20 Gy

During the fourth paradigm, the patients were asked to count mentally without speaking.

The patient received instructions before (information about paradigms) and also during (the actual instructions) the fMRI imaging session.

fMRI Image Post-Processing

All functional imaging data were processed using SPM5 software (Statistical Parametrical Mapping, Wellcome Department of Cognitive Neurology, London, England). Data series were motion corrected and smoothed with 8 mm FWHM kernel. Significantly activated voxels were identified using an initial p value threshold of 0.001. fMRI scan data (mean image) was combined with the T1 structural MRI image obtained at the same scanning position, allowing visibility of the functional MR activation color map on the patient's brain anatomy (Fig. 1).

The merged image sets (JPEG format) were then converted into DICOM format using MatLab® software. In this conversion, the color images were replaced with the grayscale images using the intensity of the green color as the grayscale intensity. fMRI DICOM series were also sent to the planning system.

Contouring, Fusion

The planning CT series, the postoperative whole-brain axial MRI series and the four fMRI series were registered in the planning system (Nucletron, ONCENTRA MASTERPLAN Version: 3.1.1.4). Using the registration-fusion tool, fMRI and conventional MRI series (T2 and T1 with contrast

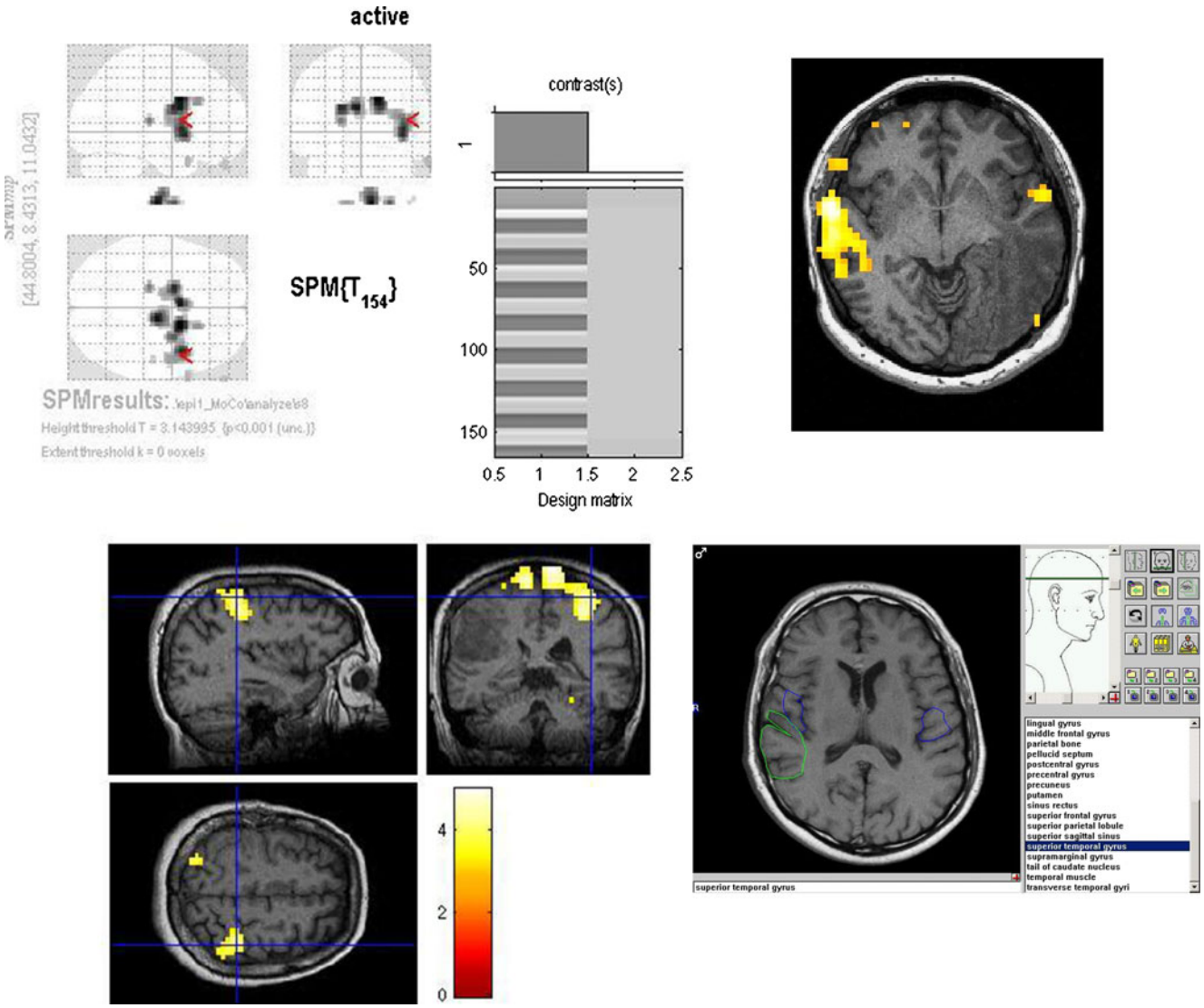

Fig. 1 fMRI Color map of right primary motor cortex in the mid temporal gyrus. Delineation of the active zone was done using the database of Schering Atlas

agent) were fused with the planning CT series. When contouring CTV and PTV and OR's the current institutional protocol has been used. The CTV (Clinical Target Volume) was defined as the postoperative tissue defect, the surrounding tissue edema and the contrast enhancing mass. PTV 2 (planning target volume) was defined as the CTV plus 2 cm. An additional 0.5-cm PTV margin was added around the PTV2 to account for treatment uncertainties (Fig. 2).

Critical organs, including right and left eyes, right and left optic nerves, optic chiasm, brain and brain stem were contoured. Additional OR's (OR-OR4) were contoured on the base of the converted fMRI activation color maps. Because of the extension of the primary tumors, fMRI based OR's were marked only on the contralateral hemisphere (these area were equal to the defined highest activation functional areas). To avoid uncertainties resulting from cortex activation, an additional 2 mm margin was added to the activation area defined on the color map [1].

Treatment Planning, Evaluation

Three independent radiation physicists were asked to develop treatment plans. Conventional OR's (optic tract, brainstem) were mutually considered in the planning process.

The first physicist created conventional 3D plans (Conformal fMRI). For this planning process OR's defined by fMRI were taken in account by the physicist. A 3 field non-coplanar plans were made (because of the need of OR sparing), with the consideration of conventional organs at risk. 40 Gy was prescribed to 99% of the isocenter of the PTV. An additional boost (3 field) of up to 60 Gy was prescribed to the CTV.

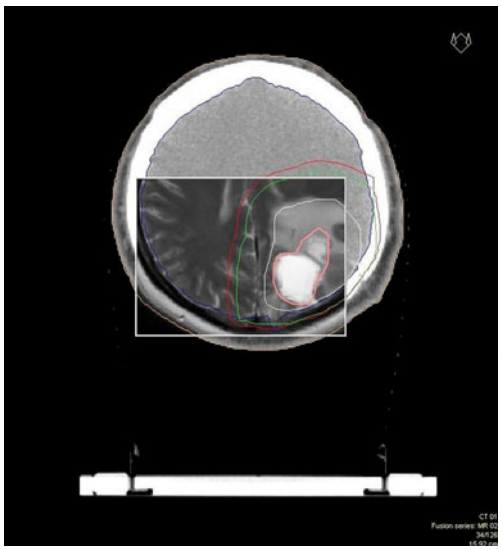

Fig. 2 Contouring after image fusion. CTV (clinical target volume-white line) was defined as the surrounding tissue edema, the postoperative tissue defect, and the contrast enhancing mass (purple line). PTV 2 was defined as the CTV plus 2 cm (green line). An additional 0.5-cm PTV margin was added around the PTV2 (red line)

The second physicist was also asked to make 3D conformal plans (Conformal), but in this case the fMRI based OR's were not taken in account by the physicist. A 2 field coplanar plan was made with the consideration of conventional organs at risk. 40 Gy was prescribed to 99% of the isocenter of PTV. An additional boost (2 filed) of up to 60 Gy was prescribed to the CTV.

The third physicist was asked to develop IMRT plans (using CMS-XIO version: 4.34.02 software, with step and shoot IMRT module). Dose prescriptions were the following: PTV: V100=40 Gy, OR-OR4: maximum dose: 10 Gy, chiasm: V5=10 Gy, V30=5 Gy, brainstem: V5=40 Gy, V30=6 Gy, optic tract: maximum dose: 10 Gy. A 7 field IMRT plan was created with 157 segments (Fig. 3). Dose-volume-histograms (DVH) were used for plan analysis. An additional boost (7 field IMRT) of up to 60 Gy was prescribed to the CTV.

For plan comparison beside the conventional dose-volume-histogram analysis, the NTCP (normal tissue complication probability) model was applied with the following factors (n: volume dependence of the organ, m: slope of the NTCP versus dose) (Fig. 4):

- Brain: reference volume: whole structure, TD50=60; n=0,25; m=0,15, biological endpoint: radionecrosis
- Brainstem: reference volume: whole structure, TD50=65; n=0,16; m=0,14, biological endpoint: radionecrosis
- Optic tract: reference volume: whole structure, TD50=65; n=0,25; m=0,14, biological endpoint: radionecrosis
- Additional OR's: reference volume: whole structure, TD50=60; n=0,25; m=0,15, biological endpoint: radionecrosis [5].

Results

The definition of the OR localization was based on the Schering digital atlas (Scheringatlas Sectional Anatomy, Version 3.0, 1996, Schering AG Berlin, Germany). The localizations were the following (Figs. 5, 6):

- OR: superior temporal gyrus
- OR2: middle temporal gyrus
- OR3: lingual gyrus
- OR4: superior frontal gyrus.

In case of patient 2 the tumor destroyed the middle temporal gyrus area, in this patient no OR2 was defined.

The coverage goal of the PTV was achieved in all planning situations. Without fMRI information, functional ORs received high dose compared to 3D with fMRI

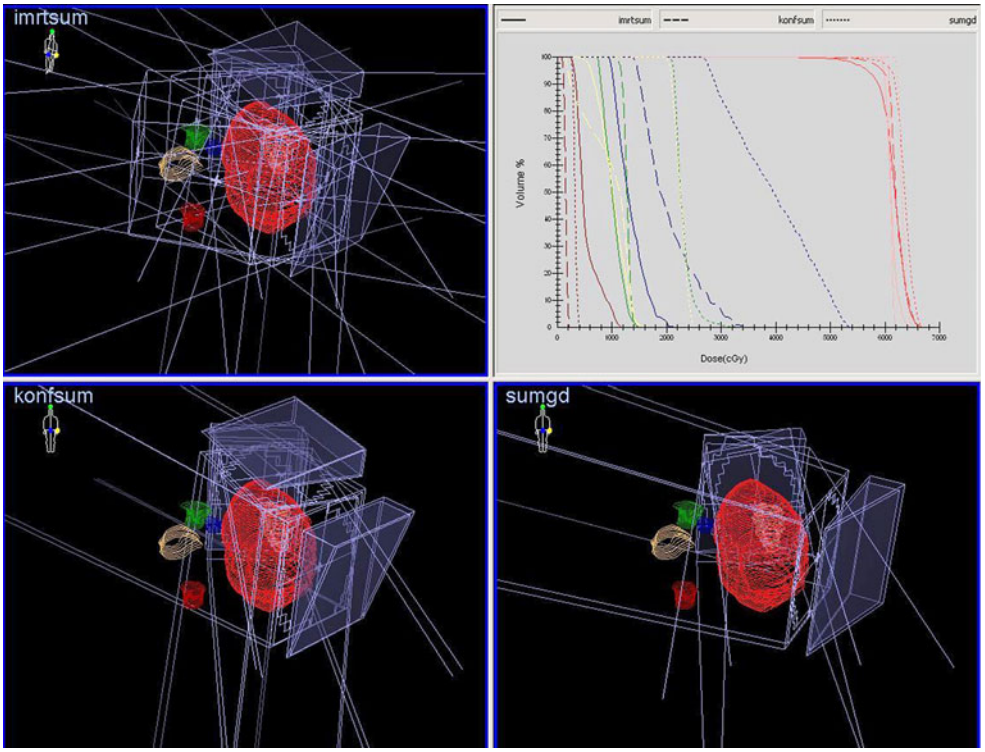

Fig. 3 Field arrangements for various treatment situations. The 7 field IMRT planning can be seen on top left image, fMRI based 3 field conformal field distribution can be seen on bottom left image and the conventional 2 field distribution on the bottom right image. Areas of the 3D reconstruction colored small red area, yellow, green and blue area demonstrate the ORs. The large red dose region represents the PTV

information and IMRT plans (OR mean dose: 29,28 Gy vs 12,53 Gy and 12,2 Gy; OR2 mean dose: 29,81 Gy vs 13,96 Gy and 14,94 Gy; OR3 mean dose: 36,24 Gy vs 16,81 Gy 14,79 Gy; and OR4 mean dose: 21,77 Gy vs 22,88 Gy and 14,79 Gy).

Using the NTCP model same results were observed in the fMRI based OR NTCP (OR mean NTCP: 2,09% vs 0% and 0%; OR2 mean NTCP: 2,83% vs 0,03% and 0%;OR3 mean NTCP: 18,31% vs 0,3% and 0%; OR4 mean NTCP: 1,35% vs 1,49% and 0,01%).

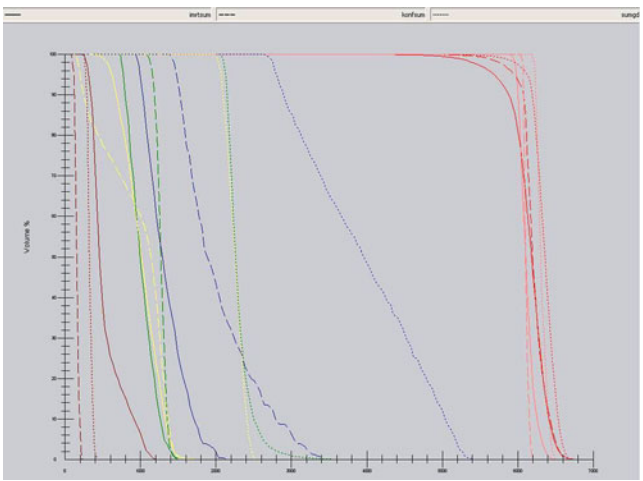

Fig. 4 Total DVH of PTV and OARs. Continuous lines represent IMRT, broken lines represent fMRI based 3D, dotted lines represent conventional 3D values. Red and pink lines show coverage of PTV and CTV. No major differences are observed considering on PTV and CTV coverage. In case of the OAR dose, the IMRT and fMRI based conformal plans show significantly better values compared to the conventional plan (blue line, green line and yellow)

IMRT allows for higher sparing of the optic tract and brainstem, compared to conventional 3D techniques (Table 2, 3, 4, 5, 6 and 7).

As these cases demonstrate, an average of 50% dose reduction was achieved in OR, OR2 and OR3 with IMRT and fMRI based 3D planning. In case of OR4 the same reduction was achieved using IMRT planning. IMRT provides additional sparing effect in the optic tract and brainstem, especially for localizations close to the midline.

Discussion

Several kinds of early and late side effects of radiotherapy can be expected during the treatment of tumors of the central nervous system [12]. The nerve tissue can be considered as functionally linked organ, therefore, impairment of certain regions may result in permanent damage to the CNS. The dose tolerance level of normal nerve tissue in case of conventional fractionated treatment (1.8-2 Gy/fractionation) is 54 Gy. In cases when this dose level is surpassed, diffuse or focal radionecrosis, leucoencephalopathy or demyelinisation may be expected [7]. Due to the fact that the dose tolerance level may be lower during radiosurgical treatments, the dose of the cranial nerves and brainstem may not reach 12–15 Gy [6]. Considering the

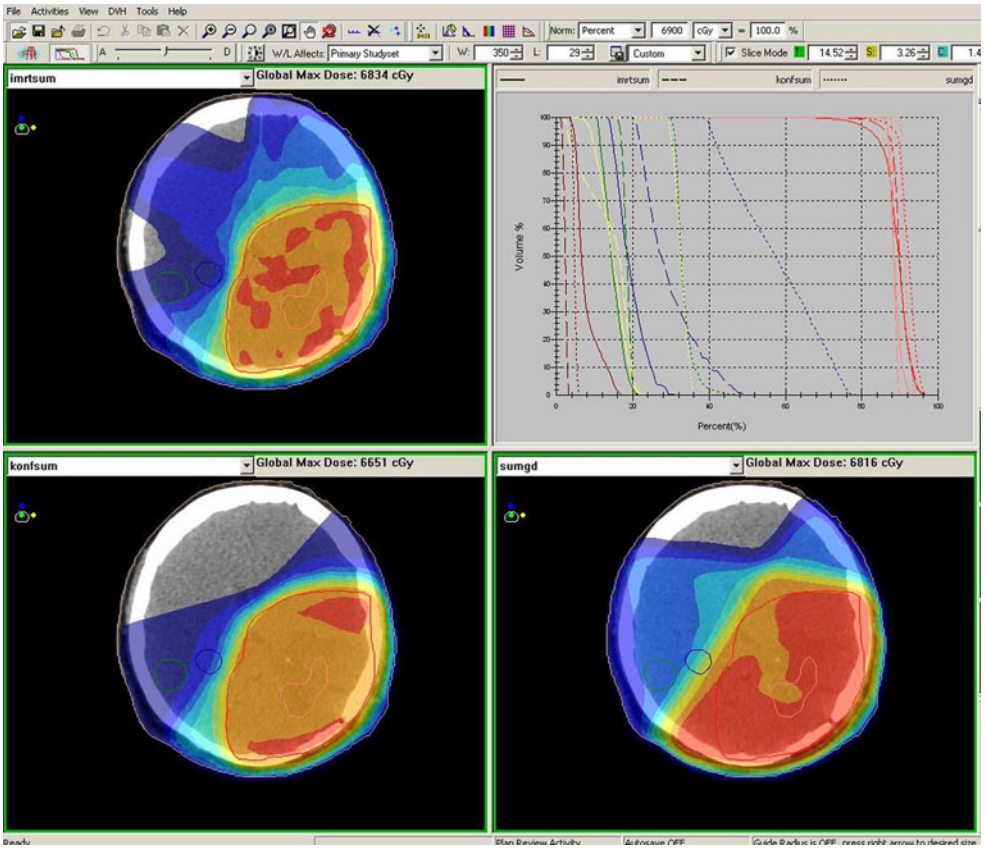

Fig. 5 ORs defined by fMRI information. OR2: mid temporal gyrus (green line), OR3: lingual gyrus (blue line). Bottom right image demonstrates the high dose area (yellow dose wash) reaching the organ at risk

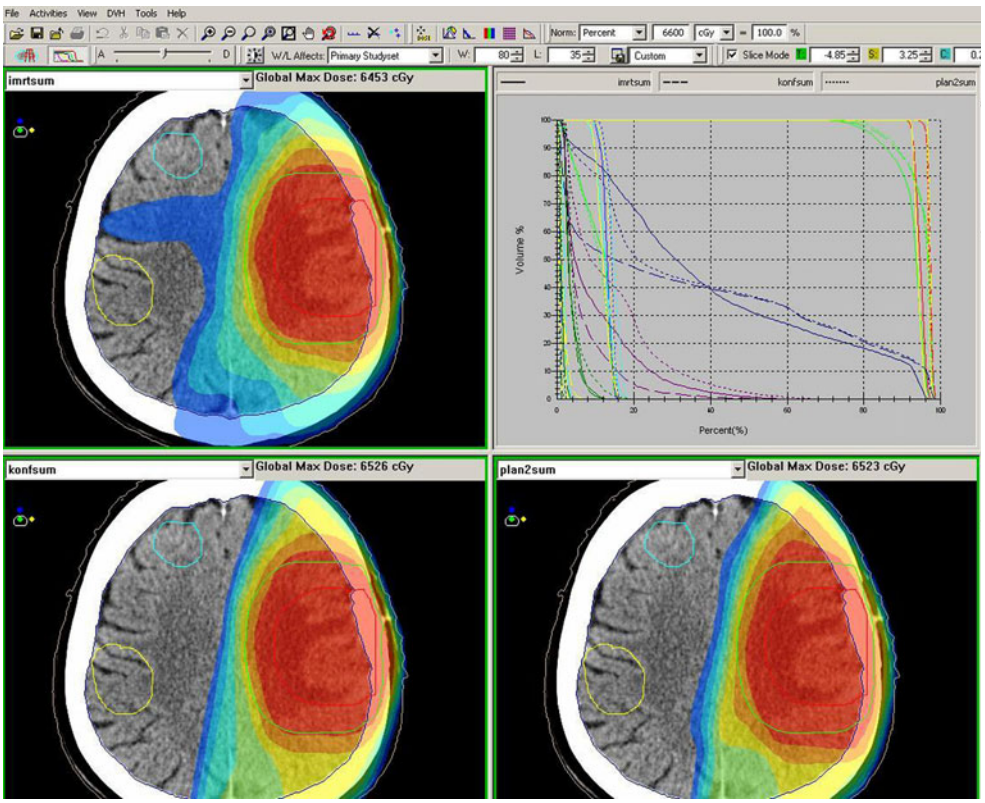

Fig. 6 ORs defined by fMRI information. OR: superior temporal gyrus (yellow line) OR4: superior frontal gyrus (purple line)

Table 2 OR and PTV mean doses in case of conformal without fMRI (white columns) and conformal with fMRI (grey columns)

Mean dose																		
Conformal without fMRI-Conformal with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4	PTV	PTV	PTV2	PTV2
Patient 1	41.74	40.73	61.91	62.1	25.60	19.3	43.66	15.34	45.90	25.12	60.40	29.41	30.42	45.63	63.16	64.01	63, 83	63.6
Patient 2	56.02	56.95	53.04	53.67	62.17	61.5	44.24	21.86	41.89	20.99	N/A	N/A	44.06	30.89	62.47	63.15	63.16	63, 99
Patient 3	26.27	23.25	9.23	4.29	24.70	19.23	6.36	0.39	9.12	0.39	8.87	0.78	9.48	1.06	63.96	64.01	63.87	64.1
Patient 4	43.85	35.86	44.15	50.12	32.91	25.64	22.84	12, 54	22.34	9.33	39.45	20.23	3.10	13.94	63.35	61.94	63.52	62.18
Mean	41.97	39.20	42.08	42.55	36.35	31.42	29.28	12.53	29.81	13.96	36.24	16.81	21.77	22.88	63.24	63.28	63.52	63.29
SD	12.21	13.94	23.07	25.99	17.60	20.28	18.23	11.01	17.21	11.25	25.91	14.62	18.90	19.47	0.61	0.98	0.36	1.00
Median	42.80	38.30	48.60	51.90	29.26	22.47	33.25	15.34	32.12	15.16	39.45	20.23	19.95	22.42	63.26	63.58	63.52	63.60

Table 3 OR and PTV mean doses in case of conformal with fMRI (white columns) and IMRT with fMRI (grey columns)

Mean dose																		
Conformal with fMRI-IMRT with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4	PTV	PTV	PTV2	PTV2
Patient 1	40.73	39.36	62.1	63.24	19.3	11.02	15.34	23.47	25.12	23.36	29.41	23.47	45.63	26.89	64.01	63.28	63.6	64.35
Patient 2	56.95	53.04	53.67	40.88	61.5	36.77	21.86	17.72	20.99	18.09	N/A	N/A	30.89	19	63.15	62.28	63, 99	63.44
Patient 3	23.25	26.46	4.29	6.34	19.23	11.42	0.39	6.62	0.39	8.39	0.78	7.74	1.06	8.1	64.01	62.3	64.1	61.95
Patient 4	35.86	38.03	50.12	29.16	25.64	15.23	12, 54	1	9.33	9.92	20.23	13.17	13.94	5.18	61.94	61.32	62.18	61.99
Mean	39.20	39.22	42.55	34.91	31.42	18.61	12.53	12.20	13.96	14.94	16.81	14.79	22.88	14.79	63.28	62.30	63.29	62.93
SD	13.94	10.88	25.99	23.72	20.28	12.25	11.01	10.23	11.25	7.05	14.62	7.99	19.47	10.02	0.98	0.80	1.00	1.17
Median	38.30	38.70	51.90	35.02	22.47	13.33	15.34	12.17	15.16	14.01	20.23	13.17	22.42	13.55	63.58	62.29	63.60	62.72

Table 4 OR and PTV mean doses in case of conformal without fMRI (white columns) and IMRT with fMRI (grey columns)

Mean dose																		
Conformal without fMRI-IMRT with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4	PTV	PTV	PTV2	PTV2
Patient 1	41.74	39.36	61.91	63.24	25.60	11.02	43.66	23.47	45.90	23.36	60.40	23.47	30.42	26.89	63.16	63.28	63, 83	64.35
Patient 2	56.02	53.04	53.04	40.88	62.17	36.77	44.24	17.72	41.89	18.09	N/A	N/A	44.06	19	62.47	62.28	63.16	63.44
Patient 3	26.27	26.46	9.23	6.34	24.70	11.42	6.36	6.62	9.12	8.39	8.87	7.74	9.48	8.1	63.96	62.3	63.87	61.95
Patient 4	43.85	38.03	44.15	29.16	32.91	15.23	22.84	1	22.34	9.92	39.45	13.17	3.10	5.18	63.35	61.32	63.52	61.99
Mean	41.97	39.22	42.08	34.91	36.35	18.61	29.28	12.20	29.81	14.94	36.24	14.79	21.77	14.79	63.24	62.30	63.52	62.93
SD	12.21	10.88	23.07	23.72	17.60	12.25	18.23	10.23	17.21	7.05	25.91	7.99	18.90	10.02	0.61	0.80	0.36	1.17
Median	42.80	38.70	48.60	35.02	29.26	13.33	33.25	12.17	32.12	14.01	39.45	13.17	19.95	13.55	63.26	62.29	63.52	62.72

Table 5 OR and PTV mean doses in case of conformal without fMRI (white columns) and conformal with fMRI (grey columns)

NTCP														
Conformal without fMRI-Conformal with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4
Patient 1	19.70%	17.99%	39.31%	38.06%	0.60%	0.10%	4.04%	0%	8.64%	0.10%	52.90%	0.89%	0.50%	5.50%
Patient 2	46.50%	48.95%	16.29%	20.02%	38.63%	34.92%	4.31%	0.01%	2.67%	0.01%	N/A	N/A	4.90%	0.46%
Patient 3	3.67%	3.48%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Patient 4	23.35%	15.92%	5.72%	11.11%	0.07%	0%	0%	0%	0%	0%	2.02%	0%	0%	0%
Mean	23.31%	21.59%	15.33%	17.30%	9.83%	8.76%	2.09%	0.00%	2.83%	0.03%	18.31%	0.30%	1.35%	1.49%
SD	17.67%	19.34%	17.35%	16.08%	19.21%	17.44%	2.41%	0.01%	4.07%	0.05%	29.98%	0.51%	2.38%	2.68%
Median	21.53%	16.96%	11.01%	15.57%	0.34%	0.05%	2.02%	0.00%	1.34%	0.01%	2.02%	0.00%	0.25%	0.23%

Table 6 OR NTCP values in case of conformal with fMRI (white columns) and IMRT with fMRI (grey columns)

NTCP														
Conformal with fMRI-IMRT with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4
Patient 1	17.99%	14.65%	38.06%	34.78%	0.10%	0%	0%	0%	0.10%	0%	0.89%	0%	5.50%	0%
Patient 2	48.95%	41%	20.02%	9.66%	34.92%	0.35%	0.01%	0%	0.01%	0%	N/A	N/A	0.46%	0.02%
Patient 3	3.48%	2.14%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Patient 4	15.92%	13%	11.11%	1.35%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Mean	21.59%	17.70%	17.30%	11.45%	8.76%	0.09%	0.00%	0.00%	0.03%	0.00%	0.30%	0.00%	1.49%	0.01%
SD	19.34%	16.50%	16.08%	16.13%	17.44%	0.18%	0.01%	0.00%	0.05%	0.00%	0.51%	0.00%	2.68%	0.01%
Median	16.96%	13.83%	15.57%	5.51%	0.05%	0.00%	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%	0.23%	0.00%

Table 7 OR NTCP values in case of conformal without fMRI (white columns) and IMRT with fMRI (grey columns)

NTCP														
Conformal without fMRI-IMRT with fMRI	Brain	Brain	Brainstem	Brainstem	Chiasma	Chiasma	OR	OR	OR2	OR2	OR3	OR3	OR4	OR4
Patient 1	19.70%	14.65%	39.31%	34.78%	0.60%	0%	4.04%	0%	8.64%	0%	52.90%	0%	0.50%	0%
Patient 2	46.50%	41%	16.29%	9.66%	38.63%	0.35%	4.31%	0%	2.67%	0%	N/A	N/A	4.90%	0.02%
Patient 3	3.67%	2.14%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Patient 4	23.35%	13%	5.72%	1.35%	0.07%	0%	0%	0%	0%	0%	2.02%	0%	0%	0%
Mean	23.31%	17.70%	15.33%	11.45%	9.83%	0.09%	2.09%	0.00%	2.83%	0.00%	18.31%	0.00%	1.35%	0.01%
SD	17.67%	16.50%	17.35%	16.13%	19.21%	0.18%	2.41%	0.00%	4.07%	0.00%	29.98%	0.00%	2.38%	0.01%
Median	21.53%	13.83%	11.01%	5.51%	0.34%	0.00%	2.02%	0.00%	1.34%	0.00%	2.02%	0.00%	0.25%	0.00%

fact that currently the dose of CNS tumors is normally between 60–66 Gy, treatment of these tumors is a major challenge for the clinician [10].

In high precision radiotherapy of the CNS malignancies, integration of modern cross-sectional and functional imaging gives new opportunities. Using this information and dedicated techniques, higher doses could be achieved in the planning target volume with lower toxicity. The degree of neurologic deficit is associated with the location and size of the radiation necrosis [8, 17]. Therefore, if functional areas are not involved in the high-dose regions, patients would be symptom-free even if they had radiation necrosis in a silent area. Precise integration of functional images is expected not only to reduce radiation injury, but also to increase the cure rate for tumors by allowing delivery of a sufficient dose without fear of adverse reactions [2].

Integration of the fMRI information into radiotherapy planning and treatment is not widely used. In his study Liu et al. describes a novel approach for the integration of the fMRI brain activation map with the treatment planning for stereotactic radio surgery (SRS). Multiple radiation arcs or static radiation beams were applied for SRS planning to avoid direct irradiation of the eloquent cortices, which achieved an average dose reduction of 32% to the eloquent cortices [11]. Another SRS study was presented by Aoyama et al. They used functional brain information, magneto encephalography and magnetic resonance axonography for 21 SRS patients. Of the 21 plans, 15 (71%) plans were modified by the radiation oncologist after reviewing the functional images; the volume receiving 15 Gy for these 15 patients was significantly reduced compared with the original plans [2].

Chang et al. published a novel study of integrating fMRI information into IMRT planning process of 3 patients with high grade astrocytoma. In the study the left and right primary motor cortexes (PMCs) were contoured as critical structures for IMRT planning. According to the demonstrated results using fMRI data in treatment planning, IMRT optimization can reduce the RT dose to the PMC regions without compromising the PTV coverage or sparing of other critical organs [4].

In our study the potential benefit of fMRI integration and the possible treatment abilities were examined. Because of the extension and volume of the investigated PTVs, ORs defined on the basis of fMRI were contoured only on the contralateral hemisphere. The margins due to uncertainties of the measurements, as recommended by the available literature, were applied when contouring the functionally active zones [1].

Using 3D conformal technique or IMRT, a significant reduction in dose of these regions can be achieved compared to 3D planning without fMRI information (Table 2, 3, 4, 5, 6 and 7). With the DICOM based data transfer ability of our planning software, high quality image fusion can maintained. In our study, a “quintuple fusion” (CT with 3 fMRI series and postoperative MR series) were applied, and this method can be easily used in all commercial available contouring-planning software.

Our results demonstrate that using fMRI information with conventional 3D based treatment planning, potentially benefits with the significant dose reduction of critical organs, yet not compromising the PTV coverage. fMRI can be widely used even in low grade cases (long life expectancies, lower acute- and late toxicity expected) and in cases with high grade astrocytomas or metastases (higher dose to PTV with better risk organ sparing). In light of our results, fMRI fusion can be used with a wide range of modern 3D based techniques from IMRT, SRS to conventional 3D conformal irradiation. Using the fMRI based information of these important regions with high precision treatment modalities we have the opportunity of radiation dose escalation in the near future. Further planning information, patient follow-up and experimental studies needed for the clarification of the real benefit of integrating fMRI into planning process.

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