

Fibre integrity and diffusivity of the pyramidal tract and motor cortex within and adjacent to brain tumour in patients with or without neurological deficits

Barbara Bobek-Billewicz¹, Gabriela Stasik-Pres¹, Krzysztof Majchrzak², Waldemar Senczenko³, Henryk Majchrzak², Marek Jurkowski⁴, Jakub Połetek¹

¹Department of Radiology, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch, Poland, ²Department of Neurosurgery in Sosnowiec, Silesian Medical University, Katowice, Poland, ³Sir Peter Mansfield Magnetic Resonance Centre, School of Physics and Astronomy, University of Nottingham, England, ⁴Nuclear Medicine and Endocrine Oncology Department, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch, Poland

Folia Neuropathol 2011; 49 (4): 262-270

Abstract

Background: Assessment of the relationship between preoperative neurological deficits and diffusion tensor imaging (DTI) parameters in patients with brain tumour within/adjacent to pyramidal tract and motor cortex. Evaluation of the difference in fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values in patients with low and high grade gliomas.

Material and methods: 20 patients with supratentorial brain tumours were divided into two groups: I with preoperative neurological deficits and II without preoperative neurological deficits. 8/20 tumours were classified as low grade gliomas, 10/20 as high grade gliomas and 2/10 as metastases. All MR examinations were performed on a 3T scanner. FA and ADC values were calculated for a precentral gyrus (PCG), a posterior limb of the internal capsule (PLIC) and a pyramidal tract (PT) ipsilateral and contralateral to the tumour side. These values were compared between patients with and without preoperative neurological deficits, with low and high grade gliomas.

Results: A statistical analysis revealed significant differences between patients with and without preoperative neurological deficits in PCGs and PTs ipsilateral to the tumour side. Separate analysis conducted in the group with preoperative neurological deficits showed significant statistical differences only in terms of FA values comparing ipsilateral and contralateral tumour side. No statistically significant difference was observed comparing FA and ADC values ipsilateral and contralateral to the tumour side in the group without preoperative neurological deficits and between patients with low and high grade gliomas.

Conclusions: There is a relation between FA and ADC values and preoperative deficits in patients with brain tumour adjacent/within the main white matter tracts. Tumour relation to the white matter tracts is more important than the glioma WHO grade.

Key words: diffusion tensor imaging, brain tumour, neurological deficit.

Communicating author:

Gabriela Stasik-Pres, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch, Wybrzeże Armii Krajowej 15, 44-101 Gliwice, e-mail: gabastasik@poczta.onet.pl

Background

Diffusion tensor imaging (DTI) is a promising technique for estimating the course, extent, and connectivity patterns of the white matter structures in the brain. Diffusion tensor imaging allows identification and characterization of white matter tracts as it provides a main eigenvector, which can be regarded as the main fibre-orientation estimate within a voxel [21,28,29]. It was found previously that a reconstruction result coincides well with known anatomy [11,15,18,35,41]. It was also proven that DTI provides information not only about correct white matter tracts' (WMTs) location but also about displacement, disintegration, disruption, and widening due to oedema or infiltration by tumour cells [4,10,36,40].

For evaluation of the magnitude and direction of water diffusion measurements, the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) are determined. ADC and FA help to characterize tissue composition, physical properties of tissue constituents, tissue microstructure and architectural organization.

Due to inherent surgical treatment of brain tumours, DTI has been used for pre- and postoperative visualization of white matter tracts in patients with space occupying lesions [3,8,9,13]. Knowledge about integrity and location of the major white matter tracts is important to achieve the best treatment result [1,4,10,22,23,25-27,32,34,38,42].

The aim of our study was to evaluate the relationship between preoperative neurological deficits and DTI parameters and to assess DTI parameters within the pyramidal tracts and motor cortex in patients with low or high grade gliomas.

Material and methods

Material

The analysed group comprised 20 patients with supratentorial brain tumours (9 females, 11 males, mean age 42.5 ± 15.5 years). Consecutive patients had MR examinations at the Radiodiagnostics Department at Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Gliwice Branch, between April 2007 and May 2008. All patients signed informed consent prior to the examination. Patients tested fell into two groups. Group I consisted of 7 out of 20 patients with neurological deficits before surgery. Group II included 13 out of 20 pa-

tients who did not present any neurological deficits before surgery. Preoperative neurological deficit was defined as a hemiparesis according to Lovett's scale. All patients underwent surgical excision of the brain tumour. Based on the histopathological examination results, patients were assigned to either a low (8/20) or high (10/20) grade glioma group. 2 out of 20 patients had metastases. All analysed tumours were at least adjacent or within the posterior limb of the internal capsule (PLIC) or precentral gyrus (PCG). It meant that between the tumour and PLIC or PCG normal appearing brain tissue was not observed. So the border of the tumour was in the close vicinity or within the reconstructed pyramidal tract. The pyramidal tract was reconstructed between the precentral gyrus and posterior limb of the internal capsule, as explained below. Different patterns of white matter tract alterations within the PLIC and PCG by the tumour were assessed according to a modified scale proposed by Jellison *et al.* [10]. White matter tracts might be deviated (type 1), oedematous (type 2), infiltrated (type 3), destroyed (type 4) or untouched (type 0) by tumour, as explained below.

Information about the tumour location relative to the pyramidal tract and precentral gyrus and the preoperative motor deficits are summarized in Table 1.

Methods

Magnetic resonance examinations were performed on a 3T scanner (Achieva, Philips) with a standard head coil.

Conventional MR imaging consisted of T1-SE (TR/TE 450/13 ms, Thk/gap 5.0/1.0 mm, FOV 230 × 230 mm, matrix 256/512), T1-3D TFE with CE (TR/TE 6.4/2.3 ms, Thk/gap 1.0/0.0 mm, FOV 256 × 256 mm, matrix 256/256), T2-TSE (TR/TE 3000/80 ms, Thk/gap 5.0/1.0 mm, FOV 230 × 184 mm, matrix 306/512), T2 FLAIR (TI = 2500 ms, TR/TE 9000/125 ms, Thk/gap 5.0/1.0 mm, FOV 230 × 182 mm, matrix 217/512).

Diffusion tensor imaging was acquired with a single-shot, spin-echo diffusion weighted echo planar imaging (EPI) TR/TE 6911/60 ms, Thk/gap 1.9/0.0 mm, FOV 224 × 224 mm, matrix 128 × 128, voxel size 2 × 2 × 2 mm. A diffusion gradient was applied along 32 directions with $b = 750 \text{ s/mm}^2$ and additional measurements without a diffusion gradient ($b = 0 \text{ s/mm}^2$) were performed. FA maps and directional DTI colour maps of the brain were generated and colour-coded

Table I. Clinical characterization of the analysed group

Patient (gender, age [years])	Brain tumour location	Histopathological diagnosis, WHO grade	Tumour location relative to PLIC and/or PCG, Type ^a	Preoperative motor deficits
1 (M, 32)	Thalamus left	Gliomatosis, IV	Adjacent, 0	None
2 (M, 33)	Frontotemporal, insula left	Astrocytoma fibrillare, II	Adjacent, 1	None
3 (F, 37)	Parietal right	Astrocytoma fibrillare, II	Adjacent, 0	None
4 (M, 20)	Frontotemporal, insula right	Astrocytoma fibrillare, II	Adjacent, 0	None
5 (F, 22)	Frontal right	Astrocytoma fibrillare, II	Adjacent, 0	None
6 (F, 18)	Temporal, insula left	DNET, I	Adjacent, 1	None
7 (F, 30)	Frontal left	Astrocytoma anaplasticum, III	Adjacent, 0	None
8 (M, 54)	Frontotemporal, insula left	Oligoastrocytoma anaplasticum, III	Adjacent, 1	None
9 (F, 34)	Frontotemporal, insula right	Astrocytoma anaplasticum, III	Adjacent, 0	None
10 (M, 56)	Temporal left	GBM, IV	Adjacent, 0	None
11 (M, 52)	Parietal left	Metastasis	Adjacent, 0	None
12 (M, 42)	Frontotemporal, insula left	GBM, IV	Adjacent, 1	None
13 (M, 72)	Temporal, insula left	GBM, IV	Adjacent, 0	None
14 (F, 58)	Frontotemporal left	Astrocytoma fibrillare, II	Within, 2/3	Hemiparesis (Lovett III), right arm and leg
15 (M, 42)	Frontal left	Astrocytoma fibrillare, II	Within, 3	Hemiparesis (Lovett IV), right arm
16 (M, 34)	Frontotemporal right, insula	Astrocytoma fibrillare, II	Adjacent, 1	Hemiparesis (Lovett IV), left arm and leg
17 (M, 38)	Frontal right	Astrocytoma gemistocyticum partim protoplasticum, II/III	Within, 3	Hemiparesis (Lovett III), left leg
18 (M, 68)	Frontoparietal right	Astrocytoma anaplasticum, III	Adjacent, 1	Hemiparesis (Lovett IV), left arm and leg
19 (F, 46)	Frontoparietal right	Astrocytoma anaplasticum, III	Within, 3	Hemiparesis (Lovett IV), left arm and leg
20 (F, 59)	Frontal left	Metastasis	Within, 2	Hemiparesis (Lovett II), right arm and leg

^aType of tumour alteration of white matter tracts by Jellison et al. – modified, 0 – no alteration, 1 – deviated, 2 – oedematous, 3 – infiltrated, 4 – destroyed, PLIC – posterior limb of the internal capsule, PCG – precentral gyrus

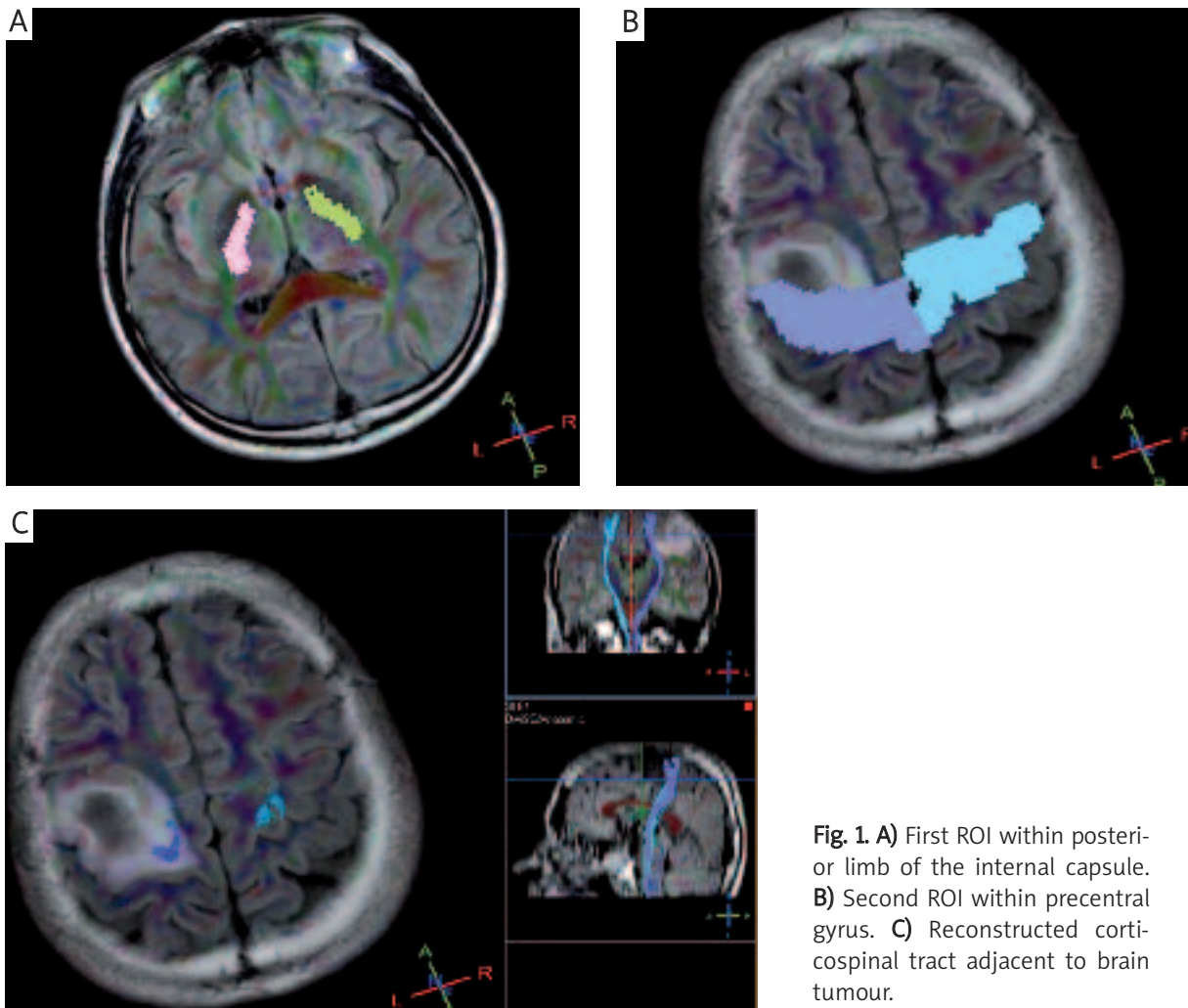


Fig. 1. A) First ROI within posterior limb of the internal capsule. B) Second ROI within precentral gyrus. C) Reconstructed corticospinal tract adjacent to brain tumour.

as to the direction of greatest diffusivity. By convention, red codes were used for right to left direction; green codes were used for anterior to posterior direction, blue codes were used for superior to inferior direction. White matter tracts were identified on directional DTI colour maps with correlation of a neuro-anatomical atlas.

Fibre tracking was performed by placing two ROIs (region of interest) on fractional anisotropy colour coded maps: the first within the posterior limb of the internal capsule (ROI_{PLIC}) and the second encapsulating the precentral gyrus ROI_{PCG} (Figs. 1A-C). Software delivered by the producer of the MR scanner was used to compute DTI parameters (FA, ADC) and to reconstruct pyramidal tracts (PT) between ROI_{PLIC} and ROI_{PCG} . Threshold values for fibre elonga-

tion were as follows: anisotropy level within voxel lower than 0.2 and deflection between the largest eigenvectors within neighbouring voxels greater than 27 degree. FA and ADC values were calculated for both hemispheres, ipsi- and contralateral side to the tumour in the precentral gyrus (PCG), the posterior limb of the internal capsule (PLIC) and a reconstructed pyramidal tract (PT): FA_PCGipsi, FA_PCGcont, FA_PLICipsi, FA_PLICcont, ADC_PCGipsi, ADC_PCGcont, ADC_PLICipsi, ADC_PLICcont). FA and ADC values for PT were mean values from reconstruction (FA_PTipsi, FA_PTcont, ADC_PTipsi, ADC_PTcont). Mean FA and ADC values were tested between patients with and without preoperative neurological deficits, with low and high grade gliomas.

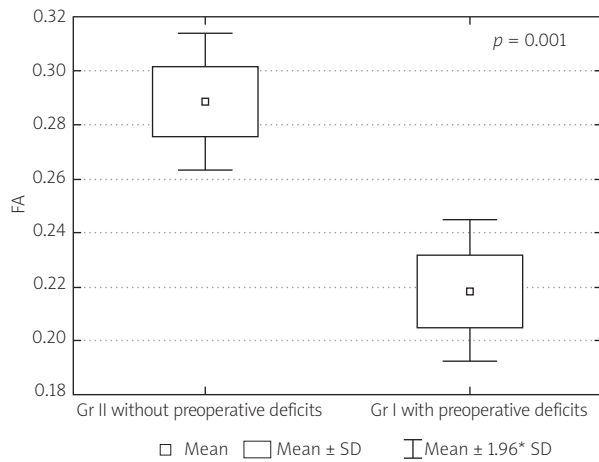


Fig. 2. Mean FA values in PCG ipsilateral to the tumour side.

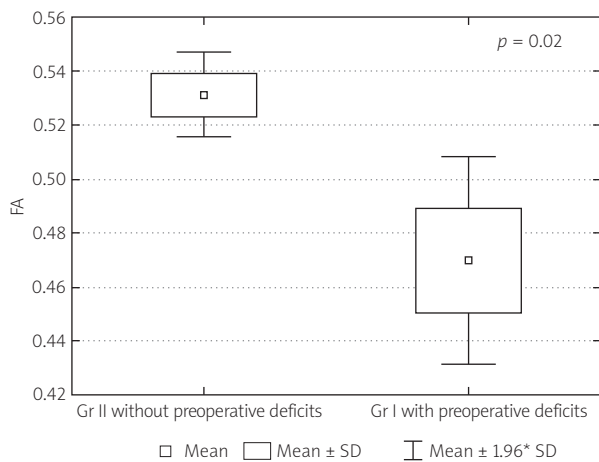


Fig. 3. Mean FA values in PT ipsilateral to the tumour side.

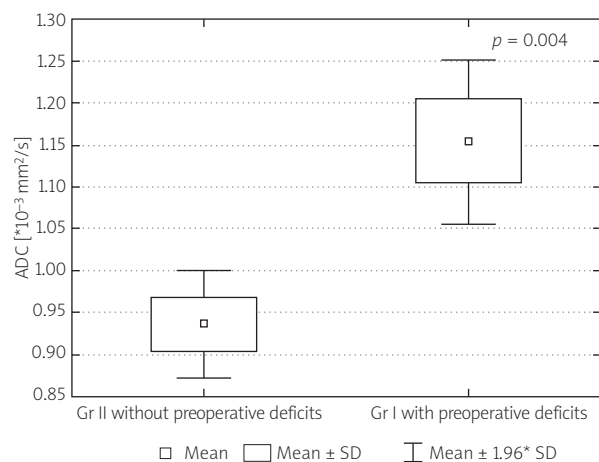


Fig. 4. Mean ADC values in PCG ipsilateral to the tumour side.

Statistical analysis

Continuous parameters with normal distribution were presented as mean \pm standard deviation (SD). The normal distribution of parameters was tested with the Shapiro-Wilk test. Mean differences were tested between patients with and without neurological deficits, with low and high grade gliomas. The significance of mean differences was tested with Student's *t*-test. Statistically significant *p*-levels were assumed as < 0.05 (two-sided). Statistical calculations and analyses were performed with Statistica PL software version 6.1 by StatSoft.

Results

Fractional anisotropy and ADC values were compared between patients with and without preoperative neurological deficits in PCGs, PLICs and PTs ipsilateral to the tumour side. Statistical analysis revealed significant differences of FA and ADC between patients with (Group I) and without (Group II) preoperative neurological deficits in PCGs and PTs ipsilateral to the tumour side. GroupI_FA_PCGipsi vs. GroupII_FA_PCGipsi (0.22 ± 0.04 vs. 0.29 ± 0.05 ; $p = 0.001$), GroupI_FA_PTipsi vs. GroupII_FA_PTipsi (0.47 ± 0.05 vs. 0.53 ± 0.03 ; $p = 0.02$), GroupI_ADC_PCGipsi vs. GroupII_ADC_PCGipsi [$(1.15 \pm 0.13$ vs. $0.94 \pm 0.12) \times 10^{-3} \text{ mm}^2/\text{s}$; $p = 0.004$], GroupI_ADC_PTipsi vs. GroupII_ADC_PTipsi [$(1.06 \pm 0.16$ vs. $0.93 \pm 0.11) \times 10^{-3} \text{ mm}^2/\text{s}$; $p = 0.05$] (Figs. 2-5). There was no difference between FA and ADC values in PLICs in both groups. We also conducted analysis separately in the group with and without preoperative neurological deficits comparing FA and ADC values ipsilateral and contralateral to the tumour side. Results showed only significant statistical differences between hemispheres in the group with neurological deficits in terms of FA values: FA_PCGipsi vs. FA_PCGcont (0.22 ± 0.04 vs. 0.3 ± 0.03 ; $p = 0.0009$), FA_PLICipsi vs. FA_PLICcont (0.52 ± 0.07 vs. 0.61 ± 0.05 ; $p = 0.02$), FA_PTipsi vs. FA_PTcont (0.47 ± 0.05 vs. 0.52 ± 0.02 ; $p = 0.03$) (Figs. 6-8). Other differences in terms of ADC values in both groups and FA values in the group without deficits were not significant between both hemispheres. The second aim of our analysis was to compare FA and ADC values in PCGs, PLICs and PTs in both hemispheres, ipsilateral and contralateral to the tumour side, between patients with low and high grade gliomas.

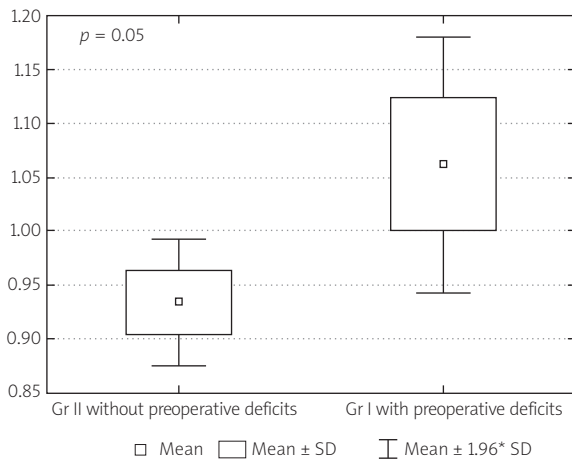


Fig. 5. Mean ADC values in PT ipsilateral to the tumour side.

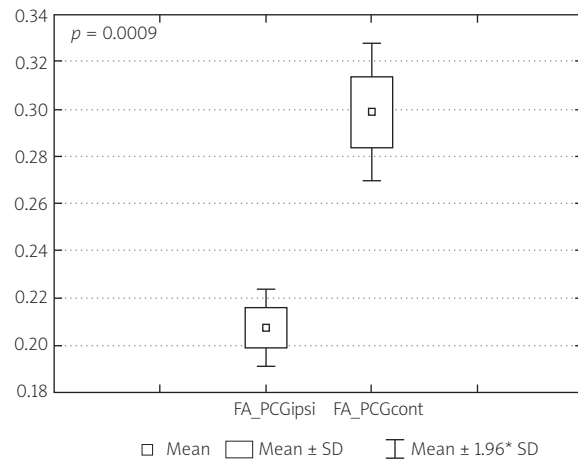


Fig. 6. Group I with preoperative neurological deficits – FA values in PCG ipsi- and contralateral to the tumour side.

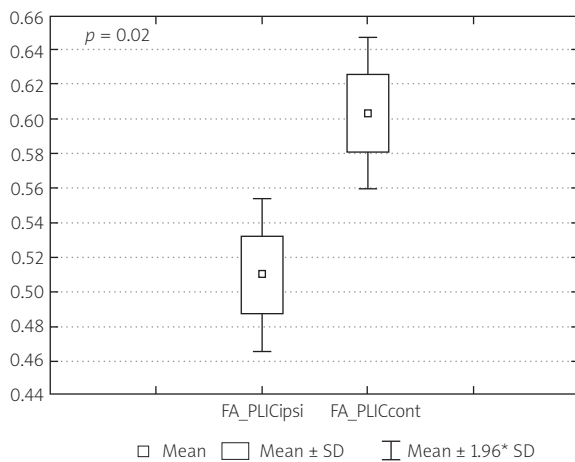


Fig. 7. Group I with preoperative neurological deficits – FA values in PLIC ipsi- and contralateral to the tumour side.

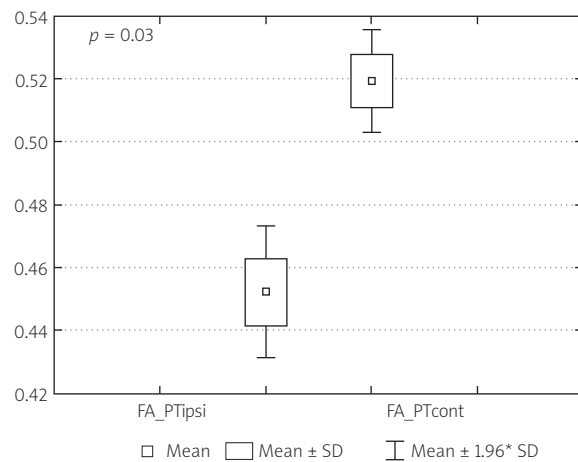


Fig. 8. Group I with preoperative neurological deficits – FA values in PT ipsi- and contralateral to the tumour side.

For this comparison metastases were excluded. No statistically significant difference was observed between the low and high grade glioma groups.

Discussion

Diffusion tensor imaging based on anisotropy of water diffusion is a method that enables detection and reconstruction of white matter tracts in the brain [2,12,14,19,20,24,37,43]. By using this MR technique one can indirectly (diffusion parameters) conclude about the influence of tumour presence on

surrounding tissues [16,30,31,33,39]. In our study we reconstructed pyramidal tracts in the brain in the vicinity and within gliomas and metastatic tumours. The outcomes of our study showed that FA values were significantly lower and ADC values were significantly higher within ipsilateral tumour side PCGs and PTs in patients with neurological deficits in comparison to ones without them. One of the explanations is the tumour relation to PTs and PCGs. Different patterns of white matter tract alterations by neoplastic tumours exist with different FA devia-

tions. Jellison *et al.* [10] proposed four patterns of white matter tract alterations by neoplastic tumours: deviated (type 1), oedematous (type 2), infiltrated (type 3), destroyed (type 4). In order to perform our analysis, another pattern was distinguished: untouched (type 0). Deviated WMT means normal or only slightly decreased FA with abnormal location, and/or direction resulting from bulk mass displacement. Field *et al.* [4] suggested the cut-off value for this pattern for FA as 25% decrease relative to the homologous tract in the contralateral hemisphere. Oedematous WMT demonstrates decreased anisotropy but their location and orientation remained normal. Infiltrated WMT shows significantly reduced anisotropy with abnormal location and/or direction but are still identifiable. Destroyed WMTs are unidentifiable on colour coded maps and show fractional anisotropy very low close to 0. Untouched WMT means normal FA with normal location relative to the homologous tract in contralateral hemisphere. It meant that the tumour bordered with the pyramidal tract. In patients with neurological deficits, tumours encapsulated more often analysed white matter tracts so the expected FA values were lower than in patients without neurological deficits. However, a significant difference was not observed in the PLICs ipsilateral to the tumour side. These mismatched results might be explained by a different tumour relation type within analysed white matter tracts at the PCG and PLIC level. Tumours were observed more often within the PCG level (type 2, 3) whereas PLICs were more often adjacent (with no alteration or type 1). Furthermore, significantly lower FA values measured ipsilaterally to the tumour side within PCGs, PLICs and PTs were obtained when comparing to FA values measured contralaterally to the tumour side in the group of patients with neurological deficits. These results also coincide well with tumour alteration of white matter tracts.

Usefulness of DTI in patients with brain tumours and neurological deficits is nowadays under research. Stadlbauer *et al.* [38] examined 20 patients with supratentorial gliomas of WHO grades II-IV before surgery. In patients suffering sensory motor deficits, the authors found significantly lower FA and higher MD values in comparison with patients without. Romano *et al.* [34] analysed white matter in the tumour's close proximity and showed that FA is significantly lower and ADC significantly higher in com-

parison to contralateral normal appearing white matter in patients with and without paresis taken altogether. After dividing the group of patients into those suffering with paresis or not, the authors obtained similar significant differences in FA and ADC values in symptomatic patients. Furthermore, the authors proved in a multiple stepwise regression that among fractional anisotropy (FA), apparent diffusion coefficient (ADC), and fibre density index (FDI), only the ADC values of white matter adjacent to the tumour showed a positive correlation with the clinical status. The authors concluded that an increased ADC reflects reduction of the number of fibres (reduced FDI) in symptomatic patients. It was found previously by Lu *et al.* [17] that for high-grade gliomas and metastatic brain tumours, mean diffusivity and FA were useful in differentiating diseased and healthy tissue. They found that mean diffusivity increased significantly and FA decreased significantly in the peritumoural signal-intensity abnormality when compared with normal-appearing white matter (NAWM). Also, they reported that the peritumoural mean diffusivity of metastases was significantly higher than that of high-grade gliomas, whereas no significant difference was noted for peritumoural FA between these two tumour types.

For comparison, low and high grade glioma group metastases were omitted. Even though no statistical significant difference was observed between low and high grade gliomas in terms of FA and ADC values in PCGs, PLICs and PTs, it seems that tumour relation to the white matter tracts is more important than the gliomas' WHO grade. On the other hand, in the paper published by Goebell *et al.* [5], the authors revealed that FA on the border of glioma GII was significantly higher than in glioma GIII, but such analysis was not the objective of our study. According to those authors, that phenomenon could be explained by preservation of major parts of neuron fibres on the border of glioma GII. Such differences were not noticeable within the centre of the tumours. The authors also claim, in a different paper, that FA and NAA (N-acetylaspartate) values reflect the integrity of the neuron fibres and the presence of neurons [6]. The highest values of FA were reached from white matter on the contralateral hemisphere to the tumour location; subsequently lower values were measured in the white matter on the ipsilateral side than on the border of the tumour range and finally the lowest values within

the tumour core. Guzman *et al.* stated that both high-grade gliomas and metastatic brain tumours have higher ADC values in the perilesional oedema than do low-grade gliomas, indicating a higher water content and greater tissue displacement due to vasogenic oedema, and probably secondary to a more aggressive histological reaction [7].

Conclusions

There is a relation between FA and ADC values and preoperative deficits in patients with brain tumour adjacent/within main white matter tracts. Tumour relation to the white matter tracts is more important than the gliomas' WHO grade.

References

1. Andrychowski J, Taraszewska A, Czernicki Z, Jurkiewicz J, Netczuk T, Dąbrowski P. Ten years observation and treatment of multifocal pilocytic astrocytoma. *Folia Neuropathol* 2009; 47: 362-370.
2. Berman JI, Mukherjee P, Partridge SC, Miller SP, Ferriero DM, Barkovich AJ, Vigneron DB, Henry RG. Quantitative diffusion tensor MRI fiber tractography of sensorimotor white matter development in premature infants. *Neuroimage* 2005; 27: 862-871.
3. Clark CA, Barrick TR, Murphy MM, Bell BA. White matter fiber tracking in patients with space-occupying lesions of the brain: a new technique for neurosurgical planning? *Neuroimage* 2003; 20: 1601-1608.
4. Field AS, Alexander AL, Wu YC, Hasan KM, Witwer B, Badie B. Diffusion Tensor Eigenvector Directional Color Imaging Patterns in the Evaluation of Cerebral White Matter Tracts Altered by Tumor. *J Magn Reson Imaging* 2004; 20: 555-562.
5. Goebell E, Paustenbach S, Vaeterlein O, Ding XQ, Heese O, Fiehler J, Kucinski T, Hagel C, Westphal M, Zeumer H. Low-grade and anaplastic gliomas: differences in architecture evaluated with diffusion-tensor MR imaging. *Radiology* 2006; 239: 217-222.
6. Goebell E, Fiehler J, Ding XQ, Paustenbach S, Nietz S, Heese O, Kucinski T, Hagel C, Westphal M, Zeumer H. Disarrangement of fiber tracts and decline of neuronal density correlate in glioma patients—a combined diffusion tensor imaging and 1H-MR spectroscopy study. *AJNR Am J Neuroradiol* 2006; 27: 1426-1431.
7. Guzman R, Altrichter S, El-Koussy M, Gralla J, Weis J, Barth A, Seiler RW, Schroth G, Lövblad KO. Contribution of the apparent diffusion coefficient in perilesional edema for the assessment of brain tumors. *J Neuroradiol* 2008; 35: 224-229.
8. Hender T, Pianka P, Sigal M, Kafri M, Ben-Bashat D, Constantini S, Graif M, Fried I, Assaf Y. Delineating gray and white matter involvement in brain lesions: three-dimensional alignment of functional magnetic resonance and diffusion-tensor imaging. *J Neurosurg* 2003; 99: 1018-1027.
9. Holodny AI, Schwartz TH, Ollenschleger M, Liu WC, Schuller M. Tumor involvement of the corticospinal tract: diffusion magnetic resonance tractography with intraoperative correlation. *J Neurosurg* 2001; 95: 1082.
10. Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL. Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns. *AJNR Am J Neuroradiol* 2004; 25: 356-369.
11. Jissendi P, Baudry S, Balériaux D. Diffusion tensor imaging (DTI) and tractography of the cerebellar projections to prefrontal and posterior parietal cortices: a study at 3T. *J Neuroradiol* 2008; 35: 42-50.
12. Jones DK, Simmons A, Williams SC, Horsfield MA. Non-invasive assessment of axonal fiber connectivity in the human brain via diffusion tensor MRI. *Magn Reson Med* 1999; 42: 37-41.
13. Laundre BJ, Jellison BJ, Badie B, Alexander AL, Field AS. Diffusion Tensor Imaging of the Corticospinal Tract before and after Mass Resection as Correlated with Clinical Motor Findings: Preliminary Data. *AJNR Am J Neuroradiol* 2005; 26: 791-796.
14. Le Bihan D, Mangin JF, Poupon C, Clark CA, Pappata S, Molko N, Chabriat H. Diffusion tensor imaging: concepts and applications. *J Magn Reson Imaging* 2001; 13: 534-546.
15. Liberatore M, Denier C, Fillard P, Frew A, Alger JR, Jen J, Perlman S, Salamon G. Diffusion tensor imaging and tractography of central pontine myelinolysis. *J Neuroradiol* 2006; 33: 189-193.
16. Lu S, Ahn D, Johnson G, Law M, Zagzag D, Grossman RI. Diffusion-tensor MR imaging of intracranial neoplasia and associated peritumoral edema: introduction of the tumor infiltration index. *Radiology* 2004; 232: 221-228.
17. Lu S, Ahn D, Johnson G, Cha S. Peritumoral Diffusion Imaging of High-Grade Gliomas and Metastatic Brain Tumors. *AJNR Am J Neuroradiol* 2003; 24: 937-941.
18. Mori S, Frederiksen K, van Zijl PC, Stieltjes B, Kraut MA, Solaiyappan M, Pomper MG. Brain white matter anatomy of tumor patients evaluated with diffusion tensor imaging. *Ann Neurol* 2002; 51: 377-380.
19. Mori S, Crain BJ, Chacko VP, van Zijl PC. Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging. *Ann Neurol* 1999; 45: 265-269.
20. Mori S, Kaufmann WE, Davatzikos C, Stieltjes B, Amodei L, Frederiksen K, Pearlson GD, Melhem ER, Solaiyappan M, Raymond GV, Moser HW, van Zijl PC. Imaging cortical association tracts in the human brain using diffusion-tensor-based axonal tracking. *Magn Reson Med* 2002; 47: 215-223.
21. Moseley ME, Kucharczyk J, Asgari HS, Norman D. Anisotropy in diffusion weighted MRI. *Magn Reson Med* 1991; 19: 321-326.
22. Nagae-Poetscher LM, Jiang H, Wakana S, Golay X, van Zijl PC, Mori S. High-Resolution Diffusion Tensor Imaging of the Brain Stem at 3T. *AJNR Am J Neuroradiol* 2004; 25: 1325-1330.
23. Nimsky C, Ganslandt O, Merhof D, Sorensen AG, Fahlbusch R. Intraoperative visualization of the pyramidal tract by diffusion-tensor-imaging-based fiber tracking. *Neuroimage* 2006; 30: 1219-1229.
24. Nimsky C, Ganslandt O, Hastreiter P, Wang R, Benner T, Sorensen AG, Fahlbusch R. Intraoperative diffusion-tensor MR imaging: shifting of white matter tracts during neurosurgical procedures – initial experience. *Radiology* 2005; 234: 218-225.

25. Nowak S, Zukiel R, Barciszewska AM, Barciszewski J. The diagnosis and therapy of brain tumours. *Folia Neuropathol* 2005; 43: 193-196.
26. Okada T, Mikuni N, Miki Y, Kikuta K, Urayama S, Hanakawa T, Fushimi Y, Yamamoto A, Kanagaki M, Fukuyama H, Hashimoto N, Togashi K. Corticospinal Tract Localization: Integration of Diffusion-Tensor Tractography at 3-T MR Imaging with Intraoperative White Matter Stimulation Mapping-Preliminary Results. *Radiology* 2006; 240: 849-857.
27. Okada T, Miki Y, Fushimi Y, Hanakawa T, Kanagaki M, Yamamoto A, Urayama S, Fukuyama H, Hiraoka M, Togashi K. Diffusion-Tensor Fiber Tractography: Intraindividual Comparison of 3.0-T and 1.5-T MR Imaging. *Radiology* 2006; 238: 668-678.
28. Pierpaoli C, Basser PJ. Toward a quantitative assessment of diffusion anisotropy. *Magn Reson Med* 1996; 36: 893-906.
29. Pierpaoli C, Jezzard P, Basser PJ, Barnett A, Di Chiro G. Diffusion tensor MR imaging of the human brain. *Radiology* 1996; 201: 637-648.
30. Price SJ, Pena A, Burnet NG, Jena R, Green HA, Carpenter TA, Pickard JD, Gillard JH. Tissue signature characterization of diffusion tensor abnormalities in cerebral gliomas. *Eur Radiol* 2004; 14: 1909-1917.
31. Provenzale JM, McGraw P, Mhatre P, Guo AC, Delong D. Peritumoral brain regions in gliomas and meningiomas: investigation with isotropic diffusion-weighted MR imaging and diffusion-tensor MR imaging. *Radiology* 2004; 23: 451-460.
32. Reich DS, Smith SA, Jones CK, Zackowski KM, van Zijl PC, Calabresi PA, Mori S. Quantitative Characterization of the Corticospinal Tract at 3T. *AJNR Am J Neuroradiol* 2006; 27: 2168-2178.
33. Roberts TP, Liu F, Kassner A, Mori S, Guha A. Fiber density index correlates with reduced fractional anisotropy in white matter of patients with glioblastoma. *AJNR Am J Neuroradiol* 2005; 26: 2183-2186.
34. Romano A, Fasoli F, Ferrante M, Ferrante L, Fantozzi LM, Bozao A. Fiber density index, fractional anisotropy, adc, and clinical motor findings in the white matter of patients with glioblastoma. *Eur Radiol* 2008; 18: 331-336.
35. Salamon N, Sicotte N, Drain A, Frew A, Alger JR, Jen J, Perlman S, Salamon G. White matter fiber tractography and color mapping of the normal human cerebellum with diffusion tensor imaging. *J Neuroradiol* 2007; 34: 115-128.
36. Sasiadek M, Szewczyk P. Imaging of the spine: New possibilities and its role in planning and monitoring therapy. *Pol Przegl Radiol* 2009; 74: 49-55.
37. Schonberg T, Pianka P, Hendler T, Pasternak O, Assaf Y. Characterization of displaced white matter by brain tumors using combined DTI and MRI. *Neuroimage* 2006; 30: 1100-1111.
38. Stadlbauer A, Nimsky C, Gruber S, Moser E, Hammen T, Engelhorn T, Buchfelder M, Ganslandt O. Changes in fiber integrity, diffusivity, and metabolism of the pyramidal tract adjacent to gliomas: a quantitative diffusion tensor fiber tracking and MR spectroscopic imaging study. *AJNR Am J Neuroradiol* 2007; 28: 462-469.
39. Stadlbauer A, Gruber S, Nimsky C, Hammen T, Gruber S, Moser E, Buchfelder M, Salomonowitz E, Nimsky C. Gliomas: histopathologic evaluation of changes in directionality and magnitude of water diffusion at diffusion-tensor MR imaging. *Radiology* 2006; 240: 803-810.
40. Szewczyk P, Trypka AE, Wojtyńska R, Leszek J, Sasiadek M. Assessment of degradation of the selected projectile, commissural and association brain fibers in patients with Alzheimer's disease on diffusion tensor MR imaging. *Pol Przegl Radiol* 2010; 75: 7-14.
41. Takahashi T, Sato N, Ota M, Nakata Y, Yamashita F, Adachi Y, Saito Y, Sugai K, Sasaki M, Asada T. Asymmetrical interhemispheric fiber tracts in patients with hemimegalencephaly on diffusion tensor magnetic resonance imaging. *J Neuroradiol* 2009; 36: 249-254.
42. Wakana S, Jiang H, Nagae-Poetscher LM, van Zijl PC, Mori S. Fiber Tract-based Atlas of Human White Matter Anatomy. *Radiology* 2004; 230: 77-87.
43. Yamada K, Kizu O, Mori S, Ito H, Nakamura H, Yuen S, Kubota T, Tanaka O, Akada W, Sasajima H, Mineura K, Nishimura T. Brain fiber tracking with clinically feasible diffusion-tensor MR imaging: initial experience. *Radiology* 2003; 227: 295-301.