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Research report

Diffusion kurtosis imaging study on temporal lobe after nasopharyngeal carcinoma radiotherapy

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ABSTRACT

Purpose: Diffusion kurtosis imaging (DKI) is a MRI technique which can measure alterations in the diffusion of water molecules to reflect tissue changes in both white and grey matter. This study evaluated the potential of DKI for the early diagnosis of radiation-induced temporal lobe changes in the grey and white matter of the temporal lobe in patients with nasopharyngeal carcinoma (NPC).
Materials and methods: Sixty patients with NPC who had normal MRI brain scans were enrolled and underwent DKI at 1 week (n=20), 6 months (n=20) or 1 year (n=20) after radiotherapy; 20 normal control individuals were also evaluated. Nonlinear fitting routines and equations were used to calculate mean diffusion (MD) and mean kurtosis (MK) and fractional anisotropy (FA). Analysis of variance was used to compare the MK/MD/FA values of white and grey matter between groups.
Results: Compared to the normal control group, grey and white matter MK values were significantly higher at 1 week after radiotherapy and significantly lower at 6 months and 1 year after radiotherapy in patients with NPC, whereas the grey and white matter MD values were significantly lower at 1 week after radiotherapy and returned to normal by 6 months and 1 year after radiotherapy.
Conclusion: DKI can be used to detect radiotherapy-induced changes in both the white and grey matter of temporal lobe in patients with NPC. MK and MD values may represent reliable indicators for the early diagnosis of radiation-induced temporal lobe changes in NPC.

1. Introduction

The areas with the highest incidence of nasopharyngeal carcinoma (NPC) are in southern China and Southeast Asia (Sarmiento and Mejia, 2014; Zhang et al., 2015). Radiotherapy is the most effective treatment for NPC (Qiu et al., 2016). However, radiation-induced temporal lobe change is a major complication observed after radiotherapy that may further develop into encephalopathy and induce neurological symptoms such as reduced neurological function and cognitive change (Chong et al., 1999; Su et al., 2011).

The precise pathogenesis of radiation-induced temporal lobe change is still under exploration, and it is complicated by the fact that clinical diagnosis is limited to pathological examinations (Chong et al., 1999; Zhou et al., 2014). Animal experiments have shown partial demyelination, vascular endothelial karyopyknosis, perivascular edema, swelling of glial cells and local nerve cell degeneration occur after whole brain radiation (Tang et al., 2006). The side effects of radiation-induced change after radiotherapy can be divided into three stages: (i) the acute stage from 24 h to 1 week after radiotherapy, when vascular endothelial cells swell, vessel wall permeability increases and acute intracranial hypertension is a common symptom. In this stage, cell and cell organelle swelling occurs, resulting in increased cell structure complexity; (ii) early delayed effects, typically occurring a few weeks to a few months after radiotherapy, usually observed as inflammation. In this stage, neuronal cell apoptosis, necrosis and nuclear disintegration can lead to decreased cell complexity; and (iii) late delayed effects occurring a few months to more than a decade after radiotherapy, such as neuronal degeneration, necrosis and gliosis, which usually manifest as irreversible neurological dysfunction. In this stage, glial cell proliferation leads to increased cell complexity, however, cell complexity does not recover to the levels observed before radiotherapy (Cheng et al., 2000; Chong et al., 1999; Lee et al., 1988; Su et al., 2011).

Currently, the prevention and treatment of radiation-induced temporal lobe change rely on early diagnosis and monitoring, with early diagnosis mainly based on radiological techniques (Lv et al., 2014; Sun et al., 2013). Enhanced MRI and magnetic resonance

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spectroscopy (MRS) techniques are both used for the diagnosis of radiation-induced temporal lobe change in patients with NPC (Wang et al., 2012). MRS can reveal metabolic changes due to radiation-induced temporal lobe change (Chong et al., 1999; Wang et al., 2012). However, the detection of abnormalities on enhanced MRI usually reflects the occurrence of irreversible radiation-induced temporal lobe change, and identification of grey matter changes due to radiation-induced temporal lobe change is currently limited to morphological measurements based on MRI.

The theory underlying DWI and diffusion tensor imaging (DTI) is based on the Gaussian diffusion behavior of water molecules (Wu and Cheung, 2010). Microstructural components in the brain, such as cell membranes, intracellular spaces and extracellular spaces, make the water distribution behave in a non-Gaussian manner. To characterize such non-Gaussian diffusion behavior, DKI, a fourth-order three-dimensional fully symmetric tensor MR imaging technique, is an extension of conventional DWI that requires the use of multiple b-values commonly up to 2000 or 3000 s/mm^2 (Minati et al., 2007; Wu and Cheung, 2010). Nervous system diseases can alter tissue microstructures that affect non-Gaussian water distribution. DKI can quantify such changes in non-Gaussian water distribution to evaluate pathophysiological changes, and has the potential to be widely applied for the diagnosis of central nervous system diseases (Giannelli et al., 2012; Grinberg et al., 2011). Application of diffusion kurtosis imaging (DKI) to assess microscopic changes in both the grey and white matter of the temporal lobe may provide useful information for the diagnosis of radiation-induced temporal lobe change.

Currently DTI is widely used to indicate white matter changes, such as ischemia and hypoxia (Gao et al., 2012), as well as developmental changes in white matter (Hui et al., 2010). However, Cheung et al. (2009) reported that DKI can reflect changes in both grey matter and white matter. Previous studies on radiotherapy-induced changes in brain tissues by Wang et al. (2009) and Chan et al. (2009) using DTI imaging indicate that changes in white matter after radiotherapy may be a major concern.

Chiang et al. used diffusion basis spectrum imaging (DBSI) to study axon/myelin integrity and white matter crossing. Axons and myelin are the major components of white matter (Chiang et al., 2014; Wang et al., 2014, 2011); however, grey matter has a high neuronal cell body cell (soma) distribution and is seldom studied. In this research, the potential of DKI as an analysis method for the early diagnosis of radiation-induced temporal lobe white matter and grey matter change was explored in patients with NPC. This study focused on the early-stage changes in grey matter and white matter during radiation-induced temporal lobe change (Table 1).

2. Results

Compared to the NC group, the grey and white matter MK values of patients with NPC were significantly higher in the 1W group ($P=0.00107$ and $P<0.001$) and significantly lower in the 6M group ($P=0.02832$ and $P<0.001$) and 1Y group (all $P<0.001$). The grey and white matter MK values of the 6M and 1Y groups were significantly lower than those of the 1W group (all $P<0.05$; Table 2; Figs. 2–4).

Compared to the NC group, the grey and white matter MD values of the 1W group of patients with NPC were significantly lower ($P=0.04804$ and $P=0.04749$). However, the grey and white matter MD values of the 6M group were significantly higher than the 1W group ($P=0.16238$ and $P=0.03779$), and the grey and white matter MD values of the 6M and 1Y groups were not significantly different to the NC group ($P=0.260236$ and $P=0.62705$; Table 3; Figs. 2–4).

Unlike the MK and MD values, clear trends were not observed

Table 1
Characteristics of the normal control (NC) group and groups of patients with NPC analyzed at one week, six months or one year after radiotherapy.

	NC	1W	6M	1Y
Number	20	20	20	20
Male:female ratio	11:9	10:10	11:9	11:9
Age (years)	49.45 ± 9.23	49.4 ± 7.88	52.9 ± 6.14	50.6 ± 3.82
Median age (years)	52.5	48	50	53
P-value*		0.98327	0.81759	0.15066
TNM stage		Number	Number	Number
	T1N1M0	1	2	1
	T1N2M0	2	0	2
	T2N1M0	6	7	8
	T2N2M0	7	7	5
	T3N1M0	2	0	1
	T3N2M0	0	3	2
	T4N1M0	2	1	0
	T4N2M0	0	0	1

* *P*-values are for comparison of age vs. normal control group.

Table 2
White matter and grey matter MK values for the normal control (NC) group and the irradiated temporal lobes of the groups of patients with NPC analyzed at one week, six months or one year after radiotherapy.

	White matter		Grey matter	
	Mean	Standard deviation	Mean	Standard deviation
NC ($n=20$)	0.90889	0.18475	0.81568	0.13949
1W ($n=20$)	1.08771	0.26214	1.05963	0.31532
6M ($n=20$)	0.59218	0.15173	0.65543	0.22763
1Y ($n=20$)	0.52089	0.14729	0.55075	0.1867
Comparison between groups		White matter *P*-value		Grey matte *P*-value
NC vs. 1W		< 0.001*		0.00107*
NC vs.6M		< 0.001*		0.02832*
NC vs. 1Y		< 0.001*		< 0.001*
1W vs. 6M		< 0.001*		< 0.001*
1W vs. 1Y		< 0.001*		< 0.001*
6M vs. 1Y		024421		0.14833

* Significant difference between groups.

Table 3
White matter and grey matter MD values for the normal control (NC) group and the irradiated temporal lobes of the groups of patients with NPC analyzed at one week, six months or one year after radiotherapy.

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1Y ($n=20$)	0.52089	0.14729	0.55075	0.1867
Comparison between groups		White matter *P*-value		Grey matte *P*-value
NC vs. 1W		0.04749*		0.04804*
NC vs. 6M		0.92101		0.5512
NC vs. 1Y		0.55871		0.08716
1W vs. 6M		0.03779*		0.16238
1W vs. 1Y		0.01114*		0.7829
6M vs. 1Y		0.62705		0.26023

* Significant difference between groups.