Diffusion in Brain Tumors
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Technique
Diffusion weighted imaging (DWI) probes the random motion of water molecules over
distances corresponding to the size of human cells and less [1]. Thus water mobility strongly
reflects tissue microstructure and its changes with physiological and pathological states.
Gradient parameters determine the sensitivity of the DWI sequence, summarized in the ‘b-
value’ with measurement at two b-values enabling calculation of an apparent diffusion
coefficient (ADC). Directional, i.e. anisotropic, water displacement is estimated from
diffusion measurements in six non colinear directions or more (diffusion tensor imaging, DTI)
and allows for calculation of the fractional anisotropy (FA), which is the degree to which
molecular displacements vary in space [2]. Following reconstruction of three-dimensional
vector field maps representing fiber orientation in each voxel, an algorithm may connect
subsequent voxels on the basis of their fiber orientation. Inference of continuity in the fibers
renders maps of ‘virtual’ fiber bundles across the brain (Diffusion Tensor Tractography, DTT).
Non Gaussian water diffusion can be modeled as the diffusional kurtosis with the kurtosis
representing the extent to which diffusion deviates from a Gaussian curve [3].

Tumor characterisation and grading
The sensitivity of DWI to cellular density and the directional organisation of tissues is
demonstrated in neuro-oncology by the relationship between ADC and tissue cellularity, with
low ADC being associated with cellular dense areas on histology [4-7]. Considerable overlap
between tumor-specific ranges of diffusion values precludes the use of ADC for a definitive
diagnosis of tumor type and grade [8]. Instead the ADC may support a diagnosis suspected
from morphological and other functional images. While ADC generally is increased in tumor
as compared to normal brain tissue, it may be decreased in lesions with very high cell density,
such as the contrast enhancing part of glioblastomas [6, 7], in contrast enhancing lymphomas
[5], in some meningiomas [6] and metastases [6, 9] as well as in medulloblastomas [10],
although to a lesser extent than in acute ischemic infarctions [8]. Low ADC and restricted
diffusion commonly differentiate epidermoids from arachnoid cysts that complete lack
structures restricting water mobility [11], and abscesses in the early phase from cystic tumors,
due to the abundance of granulocytes in pus [12]. Occasionally central necrosis of a tumor or
metastasis can show the same DWI signal characteristics as pus [13]. Use of the ADC for
differentiation of noncontrast enhancing tumor and peritumoral edema has been hampered by
overlap between tumor types. The FA is generally reduced in tumors suggesting structural
disorder, which may not add information for tissue classification. Kurtosis reportedly differs
between grade II, III and IV gliomas [14].

Preoperative mapping of white matter tracts
Delineating fiber pathways using DTI/DTT improves preoperative evaluation, planning and
surgical targeting by neuronavigation. Pathways of primary relevance in the clinic are the
pyramidal tract, the arcuate fascicle and the optic radiation. In addition to displacing,
infiltrating or destructing tracts, lesions can alter the diffusion signal: low FA due to
perilesional edema may cause failing to reconstruct fiber tracts that are invaded by tumor but
still functional when electrically stimulated.

Treatment monitoring
DWI is potentially sensitive to effects from cellular necrosis, apoptosis and membrane lysis
present before mass shrinkage of the tumor [15]. Converging evidence suggests that an
increase in tumor ADC is correlated with positive clinical response to treatment comprising chemotherapy, chemoradiation or stereotactic radiotherapy [16-18]. Greater increases in ADC in response to therapy over time have been observed in those patients alive at 1 year compared with those who died as a result of disease [19]. Moreover, the strongest predictor of 1-year survival is reportedly the volume of tumor with increased ADC after 3 weeks of treatment compared to baseline, with a larger difference in ADC predicting longer median survival. Also, pretreatment minimum ADC values are correlated with longer survival in patients with malignant supratentorial astrocytomas [20]. Tumor recurrence has been associated with an increase as well as a reduction of the ADC and is not reliably differentiated from radiation injury with DWI. In general, radiation necrosis is heterogeneous on DWI with areas of necrosis containing abundant leukocytes possibly decreasing the ADC. Normal appearing white matter adjacent to perilesional edema exhibits an increased FA ratio, relative to the contralateral side, in radiation necrosis compared to recurrent tumor [21]. During treatment with bevacizumab (Avastin®), a monoclonal antibody decreasing microvascular density and vascular permeability, ADC in contrast enhancing and non contrast enhancing tumor areas showed a stable to slightly progressive increase in non-progressors and a progressive decrease in progressors, especially early on.

This presentation will focus on the clinical application of DWI in neuro-oncology and its value for tumor characterisation and treatment monitoring.
References: