

LETTER TO THE EDITOR

In reply to letter to the editor by Dr Willems et al. re: Eccles et al. Change in diffusion weighted MRI during liver cancer radiotherapy: Preliminary observations.

CYNTHIA ECCLES¹, MASOOM A. HAIDER² & LAURA A. DAWSON³

¹CRUK/MRC Gray Institute for Radiation Oncology & Biology, University of Oxford, Oxford Cancer Centre, Churchill Hospital, Oxford, UK, ²University of Toronto, Head of Abdominal MRI, Department of Medical Imaging University Health Network, Princess Margaret Hospital and Mount Sinai Hospital, Toronto, Ontario, Canada and ³Department of Radiation Oncology, Princess Margaret Hospital, University of Toronto, Toronto, Ontario, Canada

To the Editor

Thank you to Dr Willems and colleagues for their interest in our work and their thoughtful review of the literature on diffusion weighted MRI in the treatment of liver cancers [1]. Our study [2], like those summarized by Dr Willems et al. in Table I and II found that apparent diffusion coefficient (ADC) increases early in response to therapy, and that diffusion weighted imaging (DWI) is a technique that shows promise as an early biomarker for sustained response to radiation therapy for liver cancers. Unique to our study is that we did attempt to compare ADC response to RECIST response, as shown in Figure 5 and Table II. Though difficult to draw definite conclusions from the small heterogeneous patient population, we observed the trend that the RECIST responders at one month had larger changes in ADC at one week, compared with the patients who had stable or progressive RECIST response at one month. Early ADC response was correlated with higher dose and sustained tumor response, whereas early RECIST response and volume changes on T2 MR were not, suggesting a potential benefit to DWI. As stated in our paper, "Future work to validate these preliminary findings should include greater numbers of patients categorized by diagnosis, and with more tightly maintained time-lines with smaller spans in the timing of evaluations." We agree with Dr Willems et al. that the

present level of evidence from our study and others' does not warrant the routine use of DWI imaging in response assessment.

Several challenges have plagued investigations of DWI as a biomarker for response in liver cancer, including the fact that some studies (including ours) are performed as non-mandatory companion studies to larger therapeutic studies, which makes accrual a challenge. In our experience, the majority of patients are not interested in participating in companion imaging studies, and patient drop-out before all imaging is completed is not infrequent. If additional imaging studies can be easily conducted at the time of 'routine' imaging, this may help accrual, but will not further investigations of novel imaging conducted during therapy, before standard tumor response assessment. Additionally, the standardization of DWI in liver cancer is particularly challenging, due to issues surrounding motion, and the appropriate selection of b-values and time to recovery (TR). Developments in 3D imaging and more rapid DWI techniques should help in this regard.

In summary, we strongly agree that well-designed prospective studies with standardization of imaging and follow-up protocols are needed, and we encourage future multi-institutional and co-operative group trials to incorporate imaging biomarkers in protocol design, as secondary endpoints. This will require improved collaborations between imaging scientists,

radiologists and oncologists (radiation oncologists, interventional radiologists and medical oncologists). We look forward to such studies.

Declaration of interest: The only potential conflict of interest is that “LAD has funding from Elekta (within the past year) and Bayer (active) for clinical research of radiation therapy for liver cancer patients.”

References

- [1] Willems S, Koekkoek P, Kwee T, van Der Bosch M. Diffusion-weighted MRI of the liver for early tumor response assessment: Promising technique but evidence is still lacking. *Acta Oncol* 2010 (this issue).
- [2] Eccles CL, Haider EA, Fung S, Lockwood G, Dawson LA. Change in diffusion weighted MRI during liver cancer radiotherapy: Preliminary observations. *Acta Oncol* 2009;48:1034–43.