

RE: Distinguishing between Renal Cell Carcinoma and Fat Poor Angiomyolipoma in Diffusion-Weighted Imaging

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We have read with interest the article of Ding et al. (1), entitled "Comparison of biexponential and monoexponential model of diffusion-weighted imaging for distinguishing between common renal cell carcinoma and fat poor angiomyolipoma", which was published in the Nov-Dec. 2016 issue of the journal. The study provides useful information. However, we would like to add a few comments.

Angiomyolipoma (AML), the most common tumor of mesenchymal origin, is characterised morphologically by abnormal vessels, smooth muscle cells and fatty tissue (1). It is considered as neoplasia based on the metastatic potential of some epithelioid type AMLs. Most epithelioid type AMLs are benign; but lesions with hypercellularity, atypia, and necrosis, are considered as potentially malignant

(2). Some lipid-poor AMLs are characterised by these histological features, hence, surgical treatment would be indicated, contrary to the author's suggestion that surgery is unnecessary for such cases.

In some AMLs, fusiform cells comprise the dominant component. These lesions are suggestive of leiomyoma based on appearance as well as pathological features. Restricted diffusion in renal leiomyomas has been previously reported (3). Therefore, the low apparent diffusion coefficient (ADC) values in these lesions are the result of reduced extracellular water compartment due to fusiform cells rather than the collagen excess mentioned in the article.

The authors report the occurrence of hemorrhagic and cystic areas between the cells in clear cell renal cell carcinoma (ccRCC); however, the cellular structure is more compact in lipid-poor AMLs. Thus, the structure is heterogeneous in ccRCC but homogeneous in lipid-poor AMLs. In Table 2, the authors compare the ADC and intravoxel incoherent motion parameters between the two lesions. The results indicate that the ADC and D have larger standard deviations (diffusion coefficient) in ccRCC, as compared to AMLs, thus, reflecting the lesions' microstructure more accurately than complex histogram analyses. In support of this approach to the data analyses, Hardie et al. (4), showed that standard deviations were more accurate than ADC values in distinguishing between hemangioma and metastases.

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Response

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First, we would like to express our appreciation for your valuable feedback. We agree that epithelioid type angiomyolipomas (AMLs) must be defined as potentially malignant lesions. In the introduction, we stated that "Differentiation among clear cell renal cell carcinoma (ccRCC), non-ccRCC and fat poor AML is difficult but essential for treatment planning." However, we did not mean that surgical treatment was unnecessary. Active surveillance is the accepted management for small asymptomatic masses (1). Most patients with large AMLs > 4 cm can be offered active surveillance as an initial management strategy (2). In the discussion section, we explained that "The greater cellular density and collagenous interstitial stroma that reduced water diffusion velocity might contribute to the decreased apparent diffusion coefficient (ADC) and D values of fat poor AMLs." However, we did not conduct quantitative studies on cell number and interstitial components of the renal lesions. We mainly referred to the study of Squillaci et al. (3), which suggests that while AML has significant cellularity comprising different amounts of smooth muscle and adipose tissue, the vasculature contains collagenous interstitial stroma that reduces water diffusion velocity, thus resulting in low ADC values that overlap with the ADC values of renal cell carcinoma. We considered the compact

fusiform cells (smooth muscle cells) as the main but not only reason for low ADC values. Although histogram analysis of intravoxel incoherent motion-derived parameters and the diagnostic performance were not discussed in our study, we do not agree with the comment that the use of standard deviations is more accurate than histogram analyses to evaluate the microstructure of renal lesions. Histogram analysis reflects properties of the entire lesion rather than particular slices or small regions within a slice. In addition, this method also decreases the subjectivity inherent to visual assessment of the selected region of interest and might allow better reproducibility (4).

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