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# Tumor microenvironment imaging: Benefits of multimodality to study chondrosarcoma

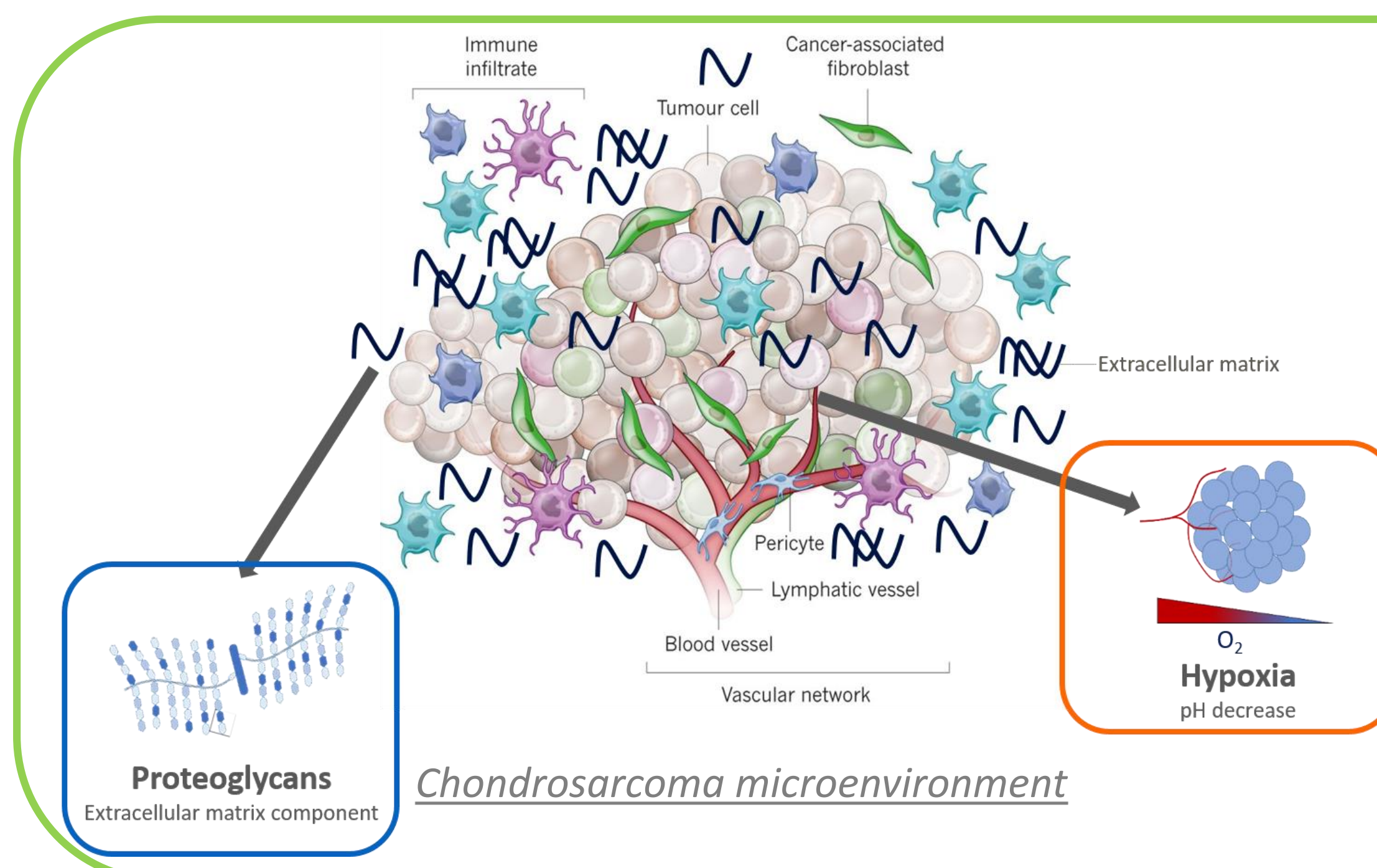
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## CONTEXT

Chondrosarcoma (CHS) is a malignant cartilaginous tumor representing the most common primary bone cancer in adults (<https://www.cancer.org/cancer/bone-cancer/about/key-statistics.html>, American Cancer Society Web site, 2021). Due to its dense chondrogenic extracellular matrix and hypoxic environment, CHS is highly resistant to conventional chemotherapy and radiation (Nazeri E *et al.*, *Crit Rev Oncol Hemat*, 2018). Development of multimodal imaging to characterize and map *in vivo* CHS microenvironment is fundamental for specific diagnosis and personalized therapy.

**In this context, we proposed to combine the resolution of chemical exchange saturation transfer (CEST) MRI with nuclear imaging sensitivity to improve CHS microenvironment understanding (Autissier R *et al.*, *Magn Reson Med*, 2021).**

## METHODS

Swarm rat CHSs were implanted subcutaneously in NMRI nude mice (n=10).

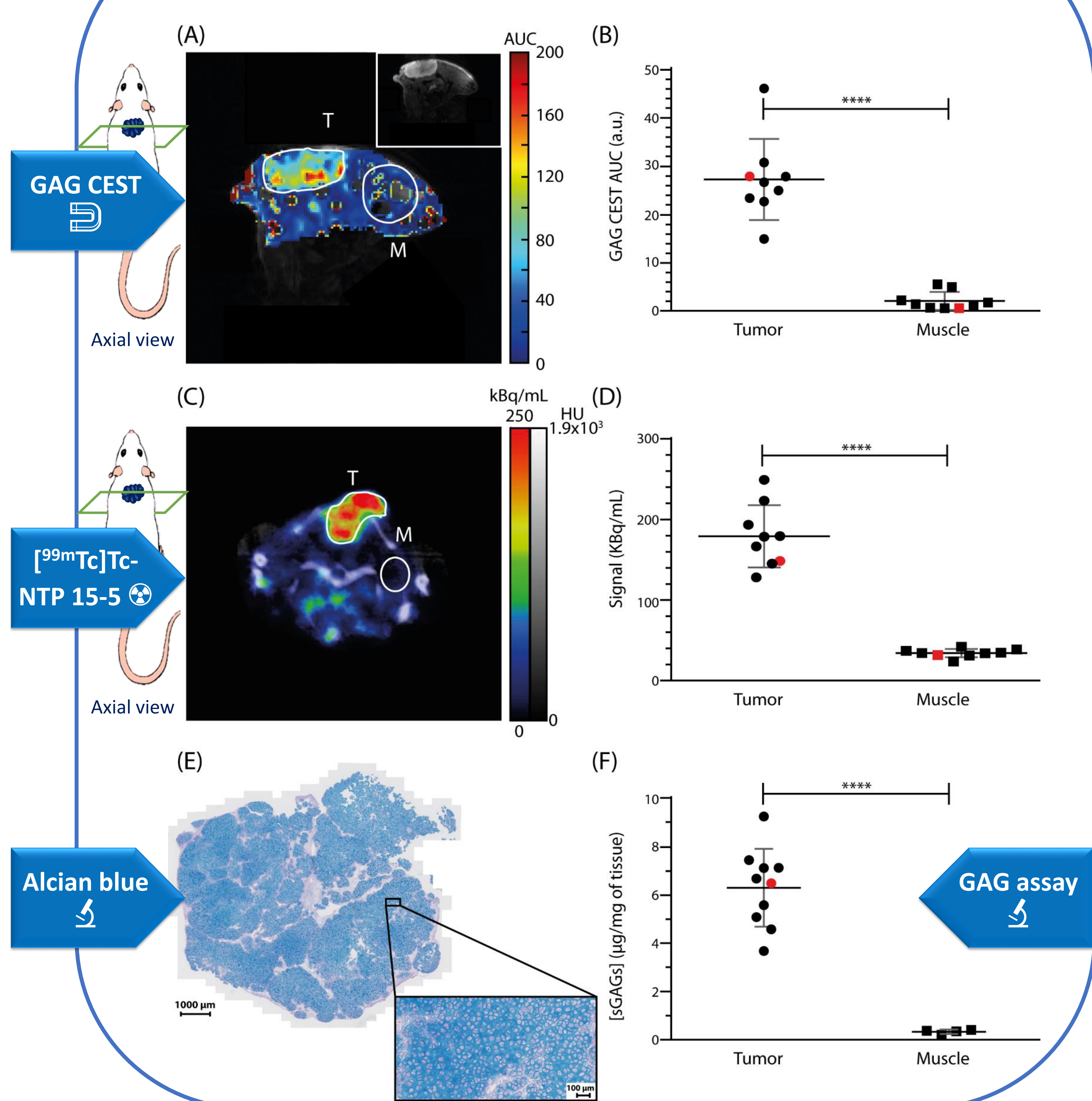
When tumors were measurable (12-16 days post-transplant), mice were imaged by CEST MRI (Dou W *et al.*, *Quant Imaging Med Surg*, 2019). Proteoglycans, the main component of chondrogenic extracellular matrix, were quantified by GAG CEST contrast. Guanidyl- and APT CEST contrasts were combined to characterize acidic pH, as hypoxia reflect.

These two features, proteoglycans and hypoxia, were assessed in parallel by nuclear imaging with [<sup>99m</sup>Tc]Tc-NTP 15-5 SPECT imaging (Peyrode C *et al.*, *Sarcoma*, 2011) and [<sup>18</sup>F]-FMISO PET imaging (Rajendran JG *et al.*, *Clin Cancer Res*, 2004), respectively.

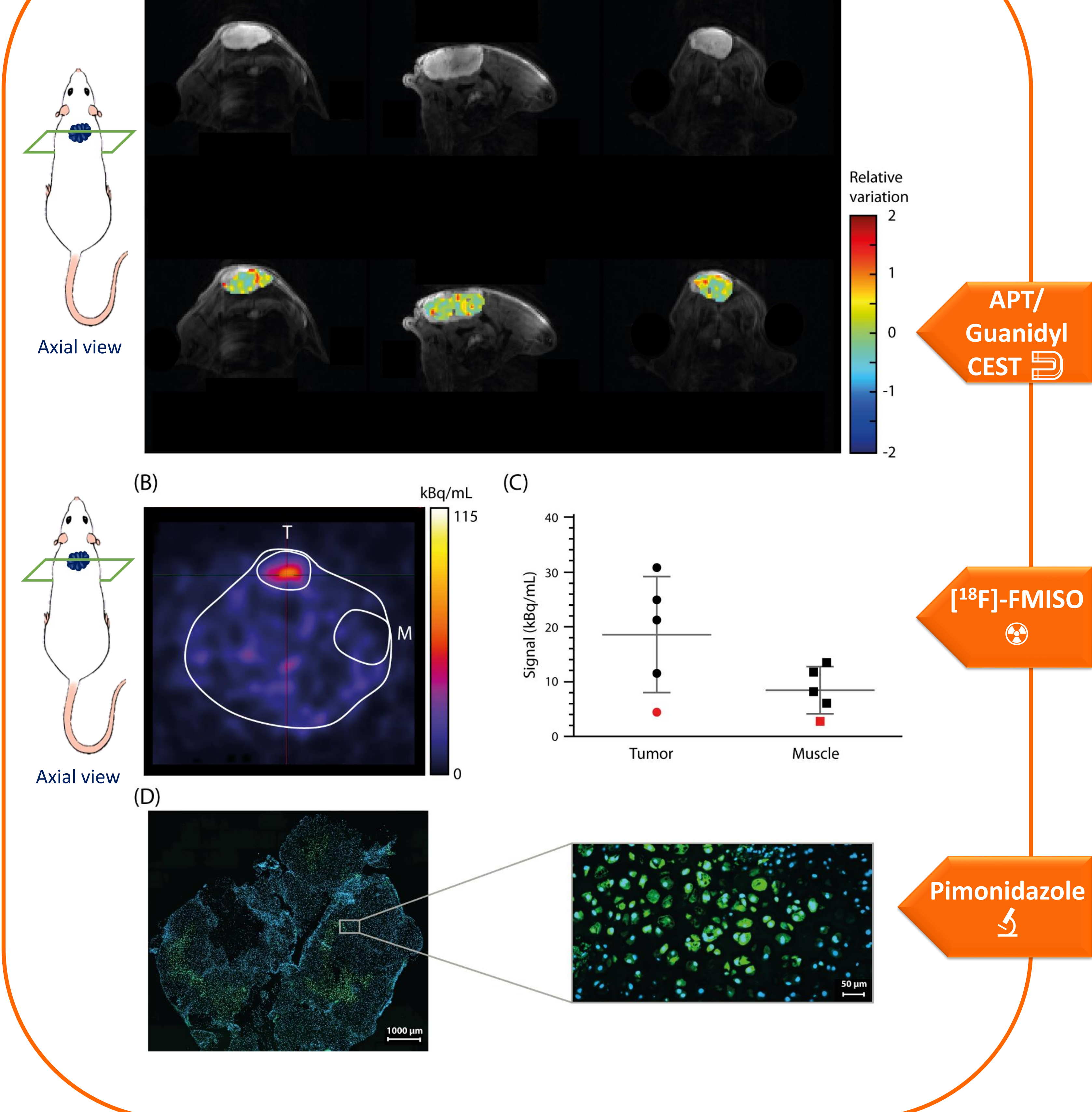
Data were also completed by *ex vivo* analyses of tumor and muscle proteoglycans (Alcian blue stain and biochemical assay with dimethylmethylene blue) and hypoxia (pimonidazole immunofluorescence).

## RESULTS

### PROTEOGLYCAN MAPPING



### HYPOXIA MAPPING



**CONCLUSION:** The results from CEST MRI, nuclear imaging and *ex vivo* analyses were in agreement and highlighted a rich proteoglycan extracellular matrix and a heterogeneous hypoxic tumoral microenvironment for Swarm rat CHS xenograft in mice.

This study emphasizes the role of multimodal imaging to characterize tumor phenotypes resistant to treatments and allows a better understanding of the relationship between tumor cells and their environment.

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