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MOTIVATION

1. Accumulation of monocytes/macrophages is the hallmark of chronic inflammation.
2. The ability to monitor this response non-invasively, in vivo, may facilitate development of new therapies.

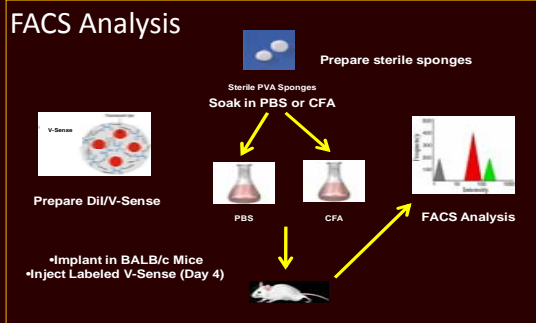
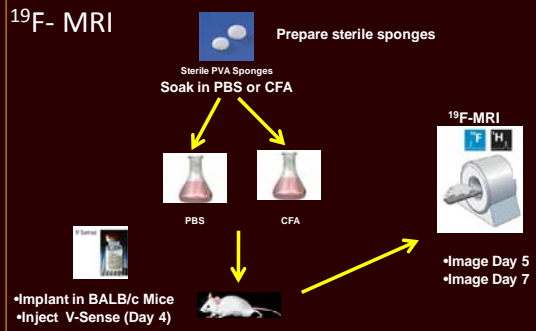
AIMS

1. Determine if the accumulation of inflammatory cells at the site of inflammation can be imaged using ¹⁹F MRI.
2. Identify the types of cells involved in inflammatory response, that uptake the PFC-nanoemulsion

BACKGROUND

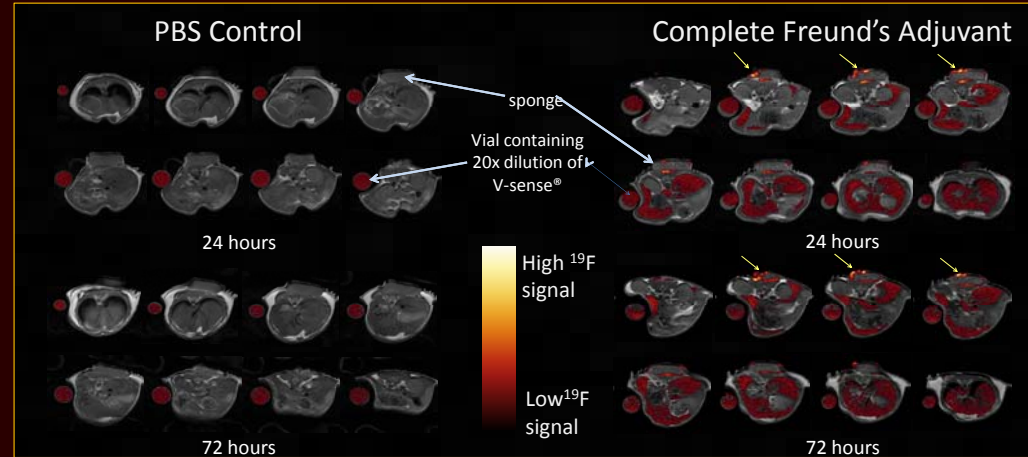
- The sponge granuloma model is a well characterized model of inflammation.
- Approaches to the non-invasive assessment of macrophage accumulation is an area of intense investigation.
- Current methods rely on PET/SPECT or MRI (with or without contrast).
- The uptake of MR active ¹⁹F nanoparticles by phagocytic cells represents an advancement in our ability to monitor an inflammatory response.
- Dil labeled PFC nanoemulsion was used to identify cells in sponges, using Fluorescence Activated Cell Sorting (FACS).

METHODS



RESULTS

¹⁹F MRI



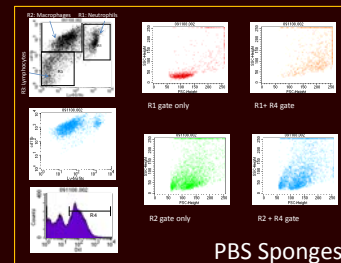
• Fluorine-19 MRI signal, indicated by the HOT color overlay on grayscale anatomical MRIs, was not detected in animals implanted with PBS soaked sponges (*Left*).

• Animals implanted with CFA-soaked sponges (*Right*) showed high ¹⁹F signal in sponges (*arrows*) and in the liver.

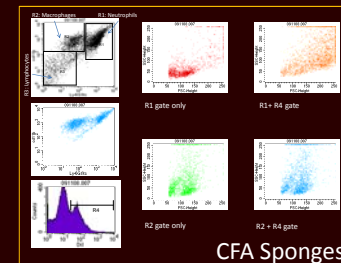
• Animals implanted with CFA soaked sponges accumulated over 10x the number of inflammatory cells relative to animals receiving PBS soaked sponges.

(Imaging Protocol: A ¹H anatomical scan was acquired using a T2-weighted spin-echo with slices covering the sponge, liver, spleen and kidneys. A ¹⁹F scan was acquired over the same slices using a fast spin echo sequence: TR/TE=4000/12.5 ms, 8 echoes per excitation, 120 averages, 64x64 matrix, 28x28mm FOV, and 1.5mm slice thickness, 1 hour imaging time)

FACS ANALYSIS



Region	%Total
R1	20
R2	55
R3	25
R4	51



Region	%Total
R1	62
R2	22
R3	13
R4	22

• Macrophages are most abundant in the PBS sponges (*Left*) while neutrophils predominate the CFA sponges (*Right*).

• Dil labeling and FACS analysis show that 2 populations of cells uptake the ¹⁹F nanoparticles:

(i) A CD11b⁺/Ly-6G⁻ population, identified as macrophages.

(ii) A CD11b⁺/Ly-6G⁺ population of very large cells. (as yet unidentified, possibly dendritic cells).

SUMMARY AND CONCLUSIONS

- Significant ¹⁹F signal was observed in the CFA-soaked sponges, consistent with local macrophage accumulation
- No ¹⁹F signals were detectable in the control PBS-soaked sponge animals
- Local inflammation with CFA results in a systemic change in macrophage phenotype as evidenced by the accumulation of ¹⁹F nanoparticles in the liver and spleen of CFA sponge bearing animals, but not in those implanted with PBS sponges.
- We conclude that ¹⁹F-based V-Sense® nanoemulsion is a specific in vivo marker for inflammation that can be used to detect and, potentially, quantify macrophage activity.