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Meeting abstract

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2105 Graphite/metal core-shell nanocrystals as MRI contrast agents to detect vascular inflammation

Hisanori Kosuge*[1], Masahiro Terashima[1], Sarah Sherlock[2], Jin Hyung Lee[3], Hongjie Dai[2] and Michael V McConnell[1]

Address: [1]Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA, [2]Department of Chemistry, Stanford University, Stanford, CA, USA and [3]Department of Electrical Engineering, Stanford University, Stanford, CA, USA

* Corresponding author

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Introduction

Noninvasive imaging of atherosclerosis may benefit from the characterization of plaque biological activity. Macrophages are ideal targets as they have a critical role in progression of atherosclerotic lesions. Novel graphite/metal core-shell nanocrystals (CN) show promising properties as MRI contrast agents for cellular imaging [1].

Purpose

To evaluate 1) CN uptake by macrophages *in vitro*, and 2) CN uptake in mouse atherosclerotic lesions *in vivo*.

Methods

Graphite/Metal core-shell nanocrystals

CN are composed of an Fe/Co core with a carbon graphite shell and phospholipid-polyethylene glycol molecules, with Cy5.5 attached for *in vivo* experiments.

In Vitro Uptake/Imaging

Mouse macrophage cells (RAW264) were incubated with ferumoxytol (Feridex), ferumoxtran-10 (Combidex), or graphite/metal core-shell nanocrystals (CN) for 24 hours, each at a concentration of 100 ugFe/ml. After incubation, 5×10^6 cells from each group were scanned by MRI at 1.5 T (GE Healthcare, Milwaukee, WI) to examine cellular uptake of contrast using a standard gradient echo sequence (TR/TE = 100/10, FA = 30, Matrix = 256 × 256, slice thickness = 2.0, FOV = 12 cm).

In Vivo Uptake/Imaging

FVB mice (N = 5) underwent a carotid-ligation procedure previously shown to produce a macrophage-rich atherosclerotic lesion. Briefly, they were given high fat diet for 4 weeks and then had diabetes induced by 5 daily intraperitoneal injections of streptozotocin. After 2 weeks of diabetes, carotid ligation of the left carotid artery was performed. Two weeks post carotid ligation, mice were given CN-Cy5.5 (8 nmol of Cy5.5) via tail vein and scanned serially over 12–48 hours using the Maestro *in-vivo* fluorescent imaging system (CRI, Woburn, MA). After final *in vivo* imaging, carotid arteries were exposed and both *in situ* and *ex vivo* imaging were performed.

Results

In vitro CN uptake by macrophages was clearly seen by T2*-weighted MRI. The area of signal loss was significantly greater ($p < 0.001$, Figure 1) for CN than ferumoxtran-10 (Combidex; common *in vivo* macrophage imaging agent). However, the uptake of CN *in vitro* was less than ferumoxytol (Feridex; common *in vitro* stem cell labeling agent).

In vivo fluorescence imaging showed limited carotid signal, but both *in situ* and *ex vivo* fluorescence imaging at 12–48 hours showed high signal from the ligated left carotid, confirming *in vivo* CN uptake in the atherosclerotic lesions (Figure 2). No evidence of CN accumulation was seen in the non-ligated right carotid arteries.

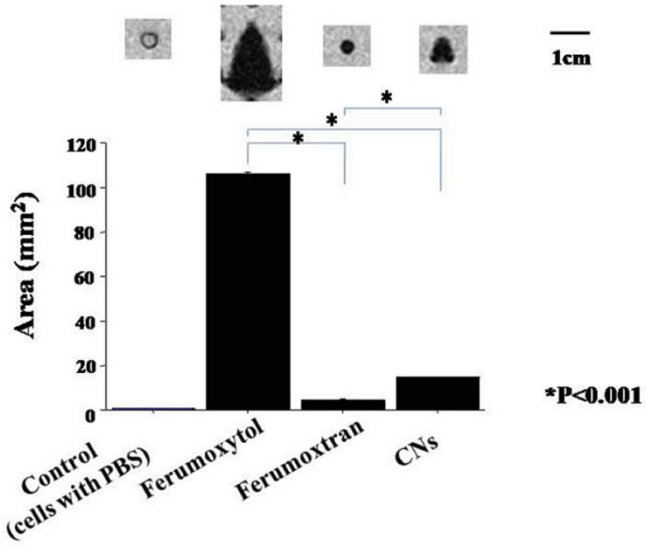

Figure 1
Contrast uptake by macrophages (T2 weighted images).

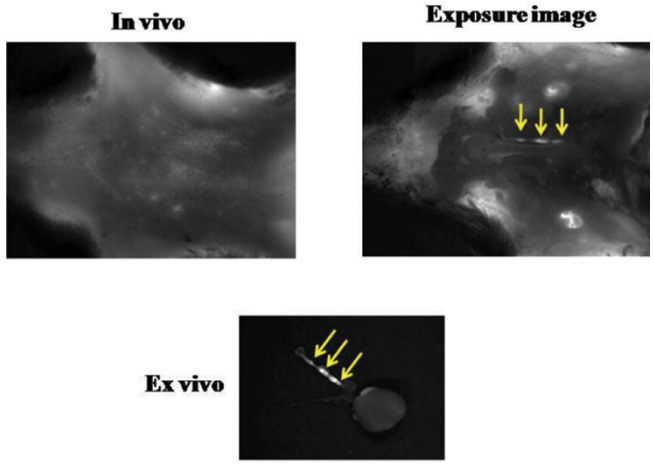

Figure 2
Fluorescence imaging in mice.

Conclusion

The novel CN contrast agent was effectively taken up by macrophages *in vitro* and by macrophage-rich atherosclerotic lesions *in vivo*. Further development of *in vivo* MRI and fluorescence imaging of graphite/metal core-shell nanocrystals may allow direct noninvasive detection of vascular inflammation.

References

1. Seo WS, *et al.*: *Nature Materials* 2006, **5:**971-976.