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## REDOX-RESPONSIVE MRI PROBES TO FOLLOW-UP THE MICROENVIRONMENT WITHIN CELL-EMBEDDING HYDROGELS

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### \*Introduction\*

In regenerative medicine, biocompatible hydrogels are increasingly used to encapsulate therapeutic cells prior to transplantation into the host to enhance their long term survival. Cell embedding within bioengineered hydrogels can shield cells from immune response and provide an optimal life-sustaining microenvironment to therapeutic cells. In addition, cell embedding offers the outstanding opportunity to insert microenvironment-responsive imaging labels within the hydrogel, paving the way for non-invasive monitoring of the extracellular microenvironment within the hydrogel. We have inserted redox-responsive MRI labels within cell-embedding hydrogels to follow-up the microenvironment redox state.

### \*Methods\*

High molecular weight chitosan polymers were chemically conjugated with a Gd-HPDO3A-chelate through a disulfide bond, and interspersed within alginate-based hydrogel capsules. Human mesenchymal stem cells (hMSCs) as model therapeutic cells were embedded into such imaging labelled hydrogel. Embedded cells were incubated under simulated hypoxia conditions, while being followed-up by T1-weighted MRI at 7T.

### \*Results\*

Under reducing conditions, reductive cleavage of the disulfide bond in the Gd-chitosan probe yields a low molecular weight Gd-chelate that eventually diffuses out of the hydrogel capsule. The resulting change of MRI contrast enhancement along time is very sensitive to the oxygenation level within cell capsules. The kinetics of clearance of contrast enhancement is an indirect indicator of the survival of encapsulated cells.

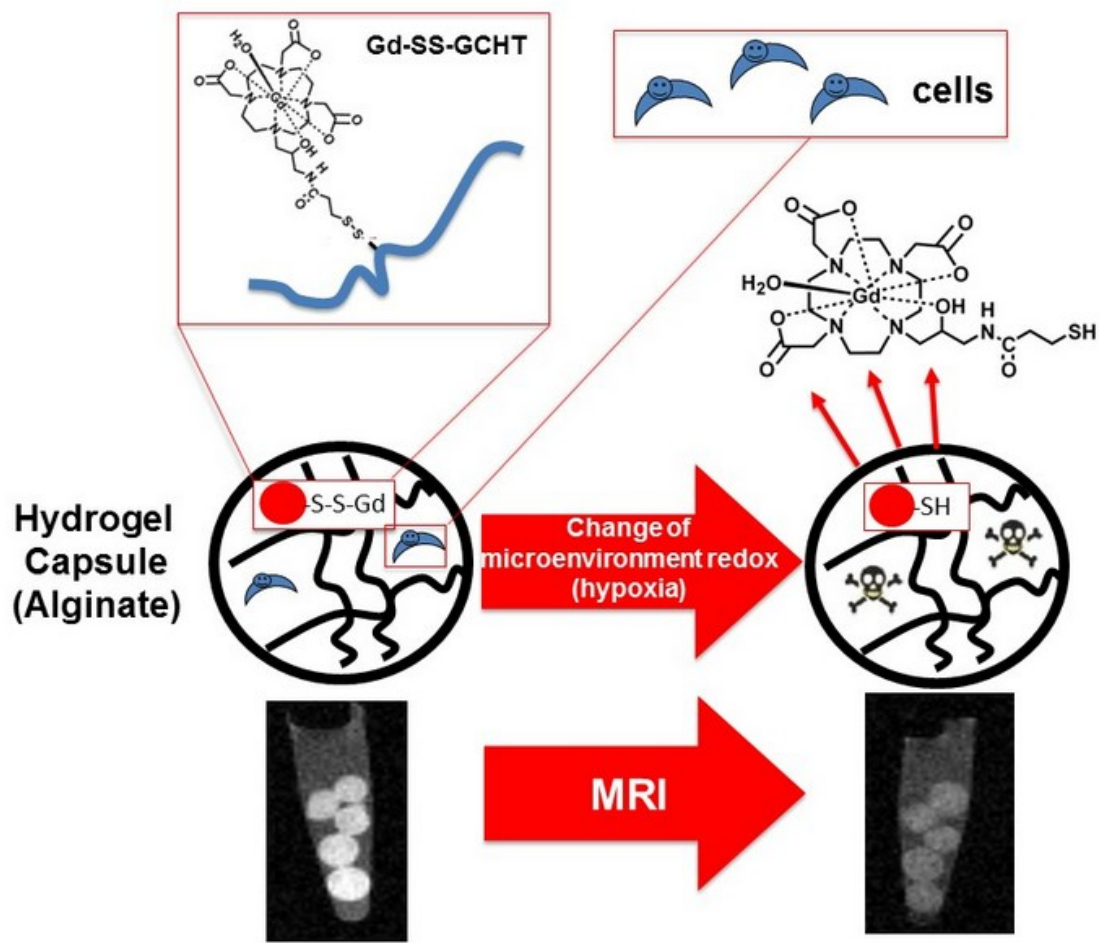
### \*Conclusions\*

The Gd-chitosan probe we developed is promising to follow-up non-invasively the redox microenvironment within cell-embedding hydrogels. This approach will find useful application to monitor whether transplanted cells succeed to restore normal tissue oxygenation levels, especially in regenerative medicine approaches to ischemic diseases.

Keywords: regenerative medicine, hydrogel, redox-responsive probe, MRI

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**Fig.1** Glycol-chitosan decorated with Gd-HPDO3A-like complexes through a disulphide bond to obtain a redox-responsive MRI probe. This probe is designed to be interspersed with therapeutic cells within hydrogel capsules, to enable the longitudinal follow-up by MRI of the redox microenvironment surrounding the embedded cells.