In vivo detection of activated platelets allows characterizing rupture of atherosclerotic plaques with molecular magnetic resonance imaging in mice

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No disclosures
Imaging targets in atherosclerosis

- Adhesion molecules
- Macrophages
- MMPs and Cathepsin
- Lipid core and Fibrous cap
- Angiogenesis
- Thrombosis
- Fibrin
- Platelets
- Vessel wall
- Tissue factor
- Thrombus
- Lipid-rich necrotic core
Targeted imaging in MRI
iron oxide particles:
- different sizes (USPIO, MPIO)
- high payload of iron
- $T_2^*$-weighted MRI (negative contrast)
- MPIOs: signal effect x50 their own diameter
  -> detection of single particles
Imaging of platelets in carotid artery thrombosis

Fibrinogen binding site

resting platelet

activated platelet

Ligand Induced Binding Sites

MPIO

LIBS single-chain Antibody + MPIO = LIBS-MPIO

A. carotis

MRI

Contrast agent injection
LIBS-MPIO or Control-MPIO

native MRI before contrast agent

MRI after contrast agent

MRI after thrombolysis

50,000 IU/kg urokinase
Imaging of platelets in carotid artery thrombosis

1.) no real plaque rupture, but an artificial model
2.) smaller thrombi?
3.) no established model of plaque rupture

--> non-invasive detection of thrombosis & monitoring of therapy

von zur Muhlen C, von Elverfeldt D et al; Circulation 2008
Model of plaque rupture in ApoE−/− mice

- Injection of contrast agent
- Scan t1
- Scan t2
- Scan t3
- Perfusion
- Histology

Timeline:
- 0 minutes
- 15 minutes
- i + 8
- i + 16
- i + 24

Arteries:
- Common carotid artery
- Internal carotid artery
- External carotid artery

Plaque and ligature

Scratching
MRI of plaque rupture & platelets in ApoE⁻/⁻ mice

LIBS-MPIO

Control-MPIO

Scratching

H1
H2
H3
H4

time

t₁

t₂

t₃
MRI of plaque rupture & platelets in ApoE<sup>-/-</sup> mice

**thrombosis >2%**

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* * p = 0.01
** ** p = 0.05
*** *** p = 0.02

**thrombosis <2%**

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§ § § p = n.s.
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Plaque rupture & platelets in ApoE−/− mice

Injured vessel

Contralateral vessel

Averaged MPIOs/section

LIBS-MPIO

control-MPIO

p < 0.01

Averaged MPIOs/section

Injured vessel

Contralateral vessel

p < 0.01
Conclusions and challenges

Conclusions

- LIBS-MPIO allows detection of activated platelets
- Application of a plaque rupture model in ApoE^/-^-mice for molecular MRI is possible
- Needle injury in this model reliably allows induction of atherothrombosis
- Atherothrombosis can be imaged in vivo by LIBS-MPIO
- Detection limit in thrombi <2% of total vessel lumen

Perspectives and challenges

- Very small thrombi and detection limit?
- Transfer from mouse to man
- Human-compatible/non-immunogenic contrast agents
Thank you very much for your attention!

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