Progress in non-invasive prediction of high risk asymptomatic carotid plaques using Bio-Optical Imaging to detect macrophage infiltration and MMPs

Clark Zeebregts
Professor of Vascular Surgery
University Medical Center Groningen
Department of Surgery
Division of Vascular Surgery
Groningen, The Netherlands

• Consultant for Vascutek
• Received research grants from W.L. Gore and Associates, LeMaitre Vascular, Atrium Maquet Getinge Group, and Cook Medical

Disclosures

Plaque development

Pivotal roles of macrophages and matrix metalloproteinases (MMPs) in the pre-rupture state


Macrophages and MMPs

• Cap thinning through involvement of immune cells (especially macrophages), SMCs, ECs by excretion of matrix degrading proteases (such as MMPs).
• MMPs have the ability to degrade extracellular matrix and collagen in the fibrous cap covering the atherosclerotic lesion, thus making the lesion vulnerable.

Principle BioOptical imaging

MMPSense in ex vivo carotid plaque

MMPSense - MMP-9

- Immunohistochemistry
- CLSM
- In-situ zymography

MMP-9 cold spot (negative)
MMP-9 hot spot (positive)

Immunohistochemistry

CLSM

In-situ zymography

18-11-2016

Distribution of MMPs in carotid plaque

- 23 excised human carotid plaques
- Incubation with MMPSense™ 680
- Near-infrared fluorescence imaging with IVIS® Spectrum
- mRNA levels of MMPs, macrophage markers, and SMCs were determined in plaque specimens, and in in vitro differentiated M1 and M2 macrophages

Multispectral optoacoustic tomography

Pulsed laser excitation

Acoustic detector

MSOT - validation with cryostate

Color stainings

Fluorescence imaging
Conclusions

- Clear need for more accurate plaque assessment as a good selection policy for intervention is quite important
- Newest imaging techniques to do so are BioOptical imaging with near infrared fluorescence and MSOT
- Main targets are macrophage infiltration, VEGF abundance, levels of matrix metalloproteinases (especially MMP-9), and calcium deposition
- Need for large population-based studies

Acknowledgements

Hendrikus Boersma
Andor Glaudemans
Reza Golestani
Niels Harlaar
Jan-Luuk Hillebrands
Nynke Jager
Daniel Razansky
Riemer Slart
René Tio
Gooitzen van Dam
Hannie Westra
Ignace Tielliu
Paul van Schaik
Jan van den Dungen
Marleen van der Laan
Bas Wallis de Vries

Thank you for your attention!