Automatic detection of amyloid plaques on ex vivo APP/PS1 mouse brain using a zoom T2-weighted spin echo sequence

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Introduction
Amyloid plaques are known as a marker of Alzheimer’s disease. They are traditionally detected as hypointense spots on T₂⁎-weighted images taking advantage of the susceptibility effect due to iron embedded inside them. However it has been recently reported that T₂ contrast might be more efficient to detect cortical amyloid plaques [1]. In this context, the goal of the present study was to compare two different strategies: (i) a conventional T₂ gradient echo sequence with volume coil [2], and (ii) a zoom adiabatic T₂ spin echo sequence with surface coil [1]. The images of an ex vivo APP/PS1 mouse brain acquired with both approaches were compared based on their ability to allow successful plaques detection using a home-made automatic procedure.

Materials and Methods

Animal protocol. A transgenic APP/PS1 mouse was sacrificed and its brain was immersed during 4 days in a solution containing 4% formalin and 2.5mM of a gadolinium-based contrast agent (Dotarem®, Guerbet, Roissy Charles de Gaulle, France), according to a 'passive staining' protocol previously established [2].

MRI acquisitions. The mouse brain was removed from the solution and placed in a container filled with Fluorinert© (3M, USA). MRI experiments were performed on a 7T small animal MRI scanner (Bruker, Ettlingen, Germany). T₂-weighted images were obtained with a 3D adiabatic zoom multi-spin echo sequence (Fig.1) (TR/TE=500/40ms, resolution=50µm³, acquisition time=11hrs) using a home-made quadrature surface coil (two 12mm-diameter loops, loaded quality factor=110). For comparison, T₂⁎-weighted images were acquired using a 3D multi-gradient echo sequence (TR/TE=100/16ms, resolution=50µm³, acquisition time=11h30) using a home-made quadrature birdcage coil (inside diameter=28mm, loaded quality factor=120).

Data processing. An automatic procedure written in Matlab (The MathWorks Inc, Natick, USA) computes local intensity gradients to detect hypointense signals in MR images and segment amyloid plaques.

Results and Discussion
Thanks to the high resolution zoom sequence combined to the increased sensitivity of surface coil, the T₂ strategy allows resolving individual amyloid plaques ex vivo (Fig. 2a, 2c and 3a) in a reasonable acquisition time, including in deep regions of the brain far from the coil.

On the T₂⁎-weighted image, cortical blood vessels also appear as hypointense signal and can disturb the detection of amyloid plaques in this area (Fig. 2b, 2d and 3b). This might explain why a better specificity to amyloid plaques is achieved when applying the segmentation algorithm on the T₂-weighted image (Fig.3).

Conclusion
In this study, we have shown that we are able to automatically localize individual amyloid plaques ex vivo on APP/PS1 mouse brain combining the zoom spin echo sequence and a dedicated segmentation procedure. The comparison with a standard gradient echo sequence reveals that T₂ contrast allows resolving amyloid plaques with a better specificity than T₂⁎ contrast, which is disturbed by the hypointense signals coming from blood vessels.

A histological study will be done to correlate amyloid plaques with MR images and confirm the present work. The next step will be to be able to detect the amyloid plaques in vivo.

References