Diffusion Tensor based Reconstruction of the Ductal Tree

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Introduction: The architecture of the ductal trees was first investigated by Sir Astley Cooper in 1840, using duct injection studies *ex-vivo* (1). Recently, computer derived tracking of whole-breast ductal trees has been achieved in few human breasts using mastectomy specimens (2). Studying the architecture of the entire ductal trees is very challenging and has not been achieved *in vivo*, yet (3, 4).

The functional breast tissue is composed of many lobes, which are highly variable in size and shape. Each lobe/system has one central duct with its peripheral branches forming a ductal tree and their associated glandular tissues. A new non-invasive MRI method for *in vivo* tracking of the mammary ductal trees using diffusion tensor imaging (DTI) was previously proposed using vector maps (5,6). Here we describe a novel methodology towards *in-vivo* determination of the entire ductal tree system.

Figure 1: Ductal Tree. Left: 3D network model of the ductal tree based on mastectomy (3). Right: Drawing of the ductal tree (1).

Methods: DTI-based fiber tracking was originally developed to track white matter of mammalian brains (7). DTI measurements of the human female breast are significantly different. Typical values of fractional anisotropy are in the range of 0.1-0.3, whereas mean diffusivities are usually higher than observed in the brain. In addition mammalian ducts show a fundamentally different topology and constitute branching trees compared to the two-point connections of neuronal tracts. In Figure 2 (left) the principal direction of the diffusion tensor is shown as an example. Due to the rather 'chaotic' distribution it is not possible to apply commonly used tracking algorithms. Therefore, we use a three step approach: I) Creating a visitmap by probabilistic tracking and accumulating the directions of the tracts/ducts (similar as done in (8)), using the nipple as seed. II) On the resulting vector field applying streamline tracking by starting at the nipple. III) Applying a clustering of the streamline tracts to obtain the tree structure as follows: First, the whole set of tracts is clustered by a hierarchical clustering scheme (MATLAB commands *linkage* and *cluster*). Usual Euclidean point-by-point distances are used to determine the distance between two tracts. The actual number of ducts depends on the 'cutoff'-parameter, which controls when a cluster is split. From mastectomy it is known that values between N=5…15 ducts are reasonable, thus, the cutoff was set accordingly. Then, each duct is iteratively subdivided into branches by a second clustering step. The branching is, again, controlled by the 'cutoff'-parameter. A branching occurs, if the tracts within one 'sub'-duct are 'too far' away (a cutoff of 1.15 is used).

Measurements were acquired on a 3T whole body MRI scanner employing a 4 channel breast array coil with b = 700 mm²/s, 64 diffusion sensitizing gradient directions, and spatial resolution = 1.9x1.9x2.0 mm³ (for more details see (5)).

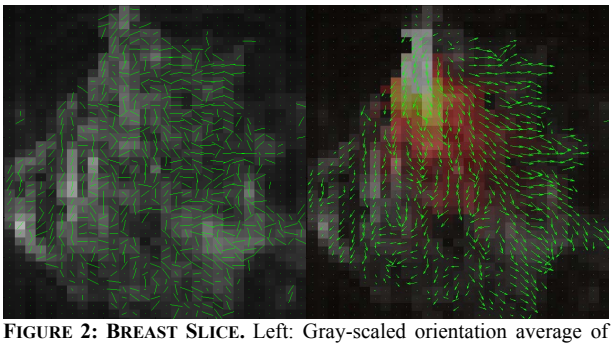

Figure 2: Breast Slice. Left: Gray-scaled orientation average of signal overlaid with the principal tensor direction. Right: Visitmap of probabilistic tracking in color, including the derived vector field.

Results:

Figure 2 (right) shows the vector-valued visitmap of the probabilistic tracking (step I). Compared to the principal direction of the diffusion tensor the field is more homogenous, but, is still keeping the underlying tissue structure. Figure 3a shows the streamline tracts relying on the vector-valued visitmap (step II). Figure 3b shows the initial ducts (N=10) obtained from the first clustering step, the thickness of the tubes indicates the number of tracts the cluster contains. Finally, in Figure 3c and 3d the ductal tree is shown. In (c) the number of initial ducts is N=10, in (d) N=6. Despite the fact that the number of initial ducts is different the results seem to be robust.

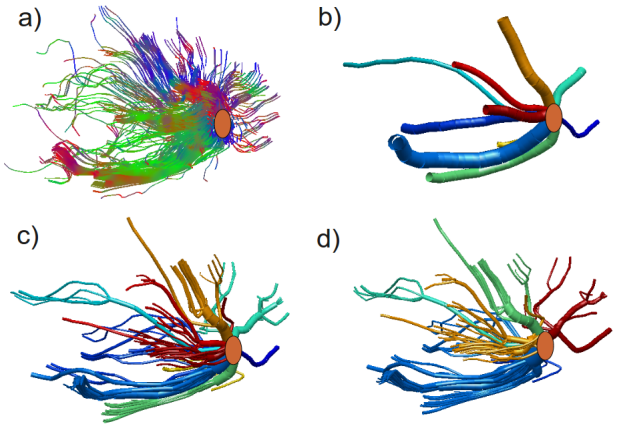

Figure 3: Ductal Tree: a) the initial stream line tracking seeded from the nipple (brown ellipse). b) Clustering into N=10 ducts, the thickness of the ducts indicate the number of tracts contained. c) The ductal tree after the final clustering step based on N=10 initial ducts. d) The ductal tree with N=6 initial ducts.

Discussion: The proposed methodology represents a first step towards *in-vivo* determination of the entire ductal tree. The preliminary results suggest that DTI is able to reveal information about the detailed, highly diversified anatomy of the mammary trees and their directional architecture towards the nipple. We found that the method is rather stable against changes of parameters, but it remains subject to future work to validate the results and analyze the parameter dependencies more carefully. It will be also important to analyze how strong the prior knowledge of all ducts starting at the nipple is influencing the results. However, the already good agreement between our results (Figure 3) and from (1) and (2) (Figure 1) is encouraging to note.

References: **(1)** J. Cooper, A.P. Anatomy of the breast, (London 1840); **(2)** Ohtake, T., et al.,Cancer 91, 2263-2272 (2001); **(3)** Love, S.M. & Barsky, S.H. Cancer 101, 1947-1957 (2004); **(4)** Going, J.J. & Moffat, J Pathol 203, 538-544 (2004); **(5)** Eyal et al, ISMRM 2010, 362, **(6)** Eyal et al, ISMRM 2008, 508, **(7)** Mori et al., Ann. Neurol. 45, 265-269 (1999); **(8)** Kreher et al , Neuroimage 43, 81-89 (2008)

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