## Validation of User Independent Planning Tool for Consistent Data Acquisition in Multi-center Trials

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**INTRODUCTION:** Success of multi-center MRI studies often depends on the consistency of the image acquisition parameters. This includes everything from briefing the subjects, subject positioning and fixation in the scanner, as well as the operator-dependent planning of the image sections to be acquired. The first is of significance to subject comfort, which will be translated directly into amount of motion artifacts. The latter is of extreme importance for the post-processing of the data where differences in angulations easily can affect the "subjective" reading by radiologists or change quantitative measures such as physical-anatomical parameters in DTI, perfusion or volumetric imaging. The problem is exacerbated in multi-slice acquisitions, especially when acquired with a gap between slices, while it is of less importance in true 3D isotropic acquisitions. The scanner vendors have recently provided automatic planning tools which can potentially improve planning consistency in between populations, centers as well as for repeated scans. In this study, we sought to evaluate the accuracy of one of these planning tools by acquiring high resolution 3D-MPRAGE images one week apart in 170 subjects located at 22 centers worldwide.

METHODS: All subjects gave written informed consent before participation according to local ethics regulations and underwent 3 high resolution 3D anatomical scans as part of the QUASAR reproducibility study\*). Any personal information from subjects was removed in accordance with local patient protection regulation (HIPAA in the US). All 22 sites were equipped with 3T Philips Achieva whole body systems with automatic planning capabilities called SmartExam [1-4]. SmartExam uses image recognition on a 3D survey for computerized identification of landmarks in the brain and is capable of automatically orienting scanning geometry based on this information. The geometrical positioning of these landmarks is derived from previous manually planned scans, in this case 10 subjects with mixed gender and race (Asians and Caucasians). This "trained" geometry database was distributed to the participating sites and all scans were planned automatically. Information about the precision of this user independent approach was obtained by co-registering MPRAGE images acquired with the following parameters: TR/TE = 6.7/3.1 ms, TI = 0.8s,  $FA = 8^{\circ}$ , res. =  $0.9x0.9x0.9mm^3$ , FOV = 240x162x190, Recon. = 288x288 and 180 slices, scan duration 5 min 26 s. The study was divided into two sessions. In session 1 two MPRAGE (1 & 2) scans where acquired with subject repositioning and subsequent automatic planning in between the two scans. Session 2 which was one week apart from session 1, consisted of a single MPRAGE (3) scan after preparation and automatic planning. Session 1 & 2 were performed in random order in ~50-50% cases. The subsequent image registration was done using ITK (The Insight Toolkit) [5] in a two step 3D rigid body registration where first a rough registration was performed based on mutual information followed by a mean square optimisation. The output of this procedure is the translation and rotation (angle and rotation axis) around the centre-of-mass of the image intensity. Choosing the rotation point in the center of the brain helps interpreting the values in a intuitive way.

**RESULTS and DISCUSSION:** The results from the registration process are summarized in Figure 1. In **a**) the combined distributions for the translations between MPRAGE 1-2, 1-3 and 2-3 are shown for the images centre-of-mass in left-right (L-R), anterior-posterior (A-P) and foot-head (F-H) directions. It can be seen that the distribution is wider in F-H (0.16 ± 1.1mm) than in A-P (0.061 ± 0.75mm) and in L-R (0.046 ± 0.48mm) direction (mean ± std.). In **b**) the distribution of rotations ( $1.5 \pm 0.6^{\circ}$ ) and **c**) the rotation axis through the centre-



Figure 1. a) Displacement distribution of the images centre-of-mass in left-right (L-R), anterior-posterior (A-P) and foot-head (F-H) directions. b) Distribution of angulations around the image centre-of-mass. Bin-size for a & b = 0.15 c) The axis of rotation in L-R, A-P and F-H directions. In red, blue and green the axis's for MPRAGE 1-2, 1-3 and 2-3 registration respectively. Notice the higher density of rotations around L-R direction. d) Typical location of the image intensity centre-of-mass around which the translation and rotation is defined.

of-mass are plotted. From c) it can be seen that the L-R axis of rotation is more prevalent than the others with an average modulus component of 0.71, 0.40 and 0.33 along L-R, A-P and F-H respectively. A reason for this directionality is likely to come from the fact that the more "natural" motion when placed supine in the scanner is rotation around the L-R axis. In addition, most motion limiting measures consist of padding and straps at the sides of the head which limits rotation to the sides but not the rotation around the L-R axis. The reason that the L-R translational distribution is narrower than the others also comes from the same fact. Furthermore, any rotation is likely to occur around a point in the back of the scull as compared to the centre-of-mass depicted in d). This would appear as an increase in the displacement in A-P and F-H direction at the centre-of-mass point. The temporal effect between the scans seems to affect the accuracy as well: The mean and std. of the resulting translation and rotation is (1.15 ± 0.38mm, 1.30 ± 0.49°) and (1.26 ± 0.44mm, 1.50 ± 0.64°) for MPRAGE1-2 and MPRAGE1-3 respectively (p<0.05). However, the increase in both displacement and rotation could be due to the fact that for session 2 the MPRAGE and SmartExam scan was acquired 5min further apart than in session 1. In general it can be argued that parts of the rotation and displacement would be due to subject movements rather than inaccuracy of the SmartExam. Generally, one would expect that the automatic planning could account for something similar to the L-R displacement (0.046 ± 0.48mm), while and angulations could be similar to the sidewise rotation (1.1 ± 0.33° where A-P & F-H component are larger than L-R). In general the accuracy is reasonably good and even though the effect of rotation is distance dependent, it would correspond to a 2mm displacement in the periphery (~1.5° and 80mm distance), while being minor nearer to the center.

**CONCLUSION:** In the present work, we evaluated the SmartExam planning for use in multi center trials. In agreement with previous reports [1-4] we found automatic planning to be effective for precise and consistent planning regardless of the location and user in charge and is likely to improve data consistency in future trials.

<sup>\*)</sup>QUASAR reproducibility study: The group includes scientists from the following sites ordered by country: Australia: Symbion Clin. Res. Imag. Centre. Belgium: Leuven University. Canada: University of British Columbia. Germany: Hospital of Schleswig-Holstein. Japan: Kumamoto University Hospital, Kyushu University, Tohoku University in Sendai. Korea: Seoul National University Bundang Hospital, Kyung-Hee University. Singapore: National Neuroscience Institute. Sweden: Lund University. Thailand: Ramathibodi Hospital. UK: Imperial College London, University of Nottingham, University of Manchester. USA: Adv. Imag. Res. Center UTSW, Columbia University, Children's Medical Center in Dallas, Johns Hopkins University/Kennedy Krieger Institute, NIH, Vanderbilt University, University of Michigan.

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