Title: Deep learning segmentation of premature neonate cerebral structures in 3D ultrasound imaging
Research Unit: CREATIS
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Abstract
This PhD thesis proposes to contribute to the development of a diagnostic brain imaging tool applicable to the entire population of prematurely born children. It concerns 2 aspects: 1) Instrumentation for the reconstruction of ultrasound volumes of the brain; 2) deep learning segmentation for the calculation of volumes of different brain structures or anomalies and comparison with measured volumes from MRI.

Context
The clinical practice in the field of preterm newborn follow-up is based on visual inspection of 2D ultrasound brain imaging (cranial ultrasound – cUS). It is the first line of testing. It takes place at the patient's bedside, is repeatable for medical follow-up (3 to 5 ultrasound exams per premature infant) and not expensive. It can be used for all preterm newborns. In case where abnormality is suspected, a 3D MRI examination is done. This concerns 10 % of the preterm newborn population but, the Epipage study (Ghada et al 2010) showed that some infants were not selected for MRI and will have brain abnormalities (irreversible motor disorder due to brain lesions or abnormal development of brain structures). To automatically quantify brain structures, cUS must be extended to 3D and diagnosis tools have to be developed for the entire population of prematurely born children (Martin et al., 2018).

Key words: medical imaging, instrumentation, reconstruction, detection, segmentation, machine learning, deep learning with weak supervision

Aim of the thesis
The goal of this PhD project is to develop methods and tools (i) to acquire 2D cUS dynamic sequence with motion sensors and to reconstruct them in 3D, (ii) to segment specific brain structures (biomarkers of cerebral development) such as thalami, basal ganglia, cerebellum and main tracts, (iii) to quantify the structures in volume and to compare them to the volumes measured with MR images of our database.

Scientific challenges
3D brain ultrasound imaging remains a key element for performing quantitative examinations. One of the ways to obtain resolution volumes compatible with brain structure segmentation is to manually scan the fontanel. We will have little annotated data, which means that we will have to develop and combine supervised and unsupervised methods. This remains crucial in medical imaging, the problem of acquiring a large amount of data and the corresponding annotations made by physicians is difficult. On the other hand, the acquisition of the images, the low contrast between structures, the speckle noise characteristic of these images lead to uncertainty about the annotations. For all these reasons, it is important to develop an automated solution whose design choices respect the constraints and conditions of use in the hospital environment.

Expected original contributions
This project will contribute to the development of quantitative brain imaging in ultrasound. We are mainly expecting:
-the development of an instrumented probe holder whose use does not disturb the doctor's usual gesture,

-development of an automatic method for volume reconstruction,
-enrichment of a pre-existing 3D ultrasound database,
-segmentation of brain structures and measurement of their volume, comparison with MRI.
These results will be obtained by methodological contributions on most recent acquisition tools (Morgan et al, 2018) and advanced deep learning tools (Dubost et al., 2019) adapted to the characteristics of brain ultrasound data, i.e.: low contrast noisy images with uncertainty on annotations (Wang et al., 2019).

Research Program
This thesis proposal is structured around three different axes which are data reconstruction, and segmentation for clinical application.
- Data reconstruction
On the reconstruction part. After a state of the art, the critical part of the existing reconstruction method (Martin et al., 2018) will be taken over for optimization and automation with the aim of transferring this part into a software tool for physicians. Two approaches have recently been published: the first is based on a learning solution (Prevost et al., 2018). The second consists in instrumenting the probe with an accelerometer and a gyrometer in order to obtain accurate reconstructions (Morgan et al., 2018). It also avoids the constraints of optical (clear field of view) and electromagnetic (limited magnetic field range and sensitivity to metallic objects/electronic devices) sensor solutions. From a methodological point of view, a study and analysis of the medical procedure during ultrasound examinations will be carried out. The aim of this step is to determine the amplitudes of the movements and the efforts applied on the patient's skull by the doctor during these examinations in order to define the working space and to dimension a robot probe holder. Once instrumented, the automated piloting of the latter will allow the images of the probe to be synchronized with the positioning and orientation sensors envisaged.
- Data segmentation
After a state of the art on segmentation methods by statistical learning, several supervised architectures will be implemented and compared on the simplest and most numerous annotated data (e.g. thalamis). This repository will be used to test advanced architectures taking into account the low number of data and the uncertainties on the annotations (case of tracts). The software bricks developed will be available on the VIP platform of the CREATIS laboratory (https://www.creatis.insa-lyon.fr/vip/) to allow access to our medical partners.
- Clinical application
The developed algorithms will be applied to the 3D ultrasound images of 30 premature neonates. For each child, three serial ultrasound volumes are planned and one of them is synchronized with a MRI exam with segmentation to be compared with the ultrasound segmentation. The three ultrasound images will be used to assess the automatic volumetric segmentation as a biomarker of the cerebral development and, the detection of fiber failure of the corticospinal tract, as a marker for a prognostic model.

Scientific supervision
The PhD student will be supervised by Philippe Delachartre (Prof, INSA Lyon). The PhD student will benefit from the expertise of:
-Philippe DELACHARTRE in segmentation of ultrasound imaging,
-Yuemin ZHU in reconstruction and segmentation, MR imaging,
-Minh Tu PHAM and Richard MOREAU (Ampere lab INSA Lyon) have skills in the design and control of mechatronic systems, complementary to those of the CREATIS supervisors. They are essential for the realization of the mechatronic part of the system,
-Dr Philippe QUETIN, pediatrician at the Avignon hospital center for data acquisition and analysis.

Use of research results

The results of this project will be presented at top machine learning and medical imaging venues as well as at the dedicated workshops concerning their intersections. The extended experimental evaluations will be submitted to top peer machine learning and medical imaging journals. On the other hand, the developed algorithms will be implemented and made available on dedicated software to be developed allowing users to perform their own clinical research using the algorithms on the collected data sets or on their own database. We expect these new methods to have a strong impact on the work of the scientists involved from the medical imaging community to analyze different kinds of ultrasound data they routinely acquire and that is clearly in demand for quantitative results of cerebral development and prognostic of all preterm newborns.

Pre-requisite qualifications of the applicant

The candidate should ideally have good instrumentation skills and a solid knowledge of deep learning methods. Good programming skills are also required (python and deep learning library) as well as a taste for experimentation on mechatronic prototypes. We are looking for an enthusiastic and autonomous student, highly motivated and interested in multidisciplinary research.

Skills developed by the successful candidate during the PhD project

The multidisciplinary aspects of the project will allow the PhD student to develop his or her capacity for openness and synthesis. Skills in deep learning for medical imaging but also in the design and control of mechatronic prototypes will be developed. Due to the theoretical and practical aspects of this proposal, the successful PhD student will be able to join research departments in both industry and academia.

Objectives for the valorization of research work

Submission of papers to the main international conferences in the field (MICCAI, MIDL, ICRA, IROS) and to the international journals of medical image analysis (IEEE Trans Medical Imaging, Medical Image Analysis, ...) and medical robotics (IEEE Transactions on Medical Robotics, ...). Given the strong application component of the topic, transfer activities to the community will also be targeted, via the development and distribution of software solutions.

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Figure

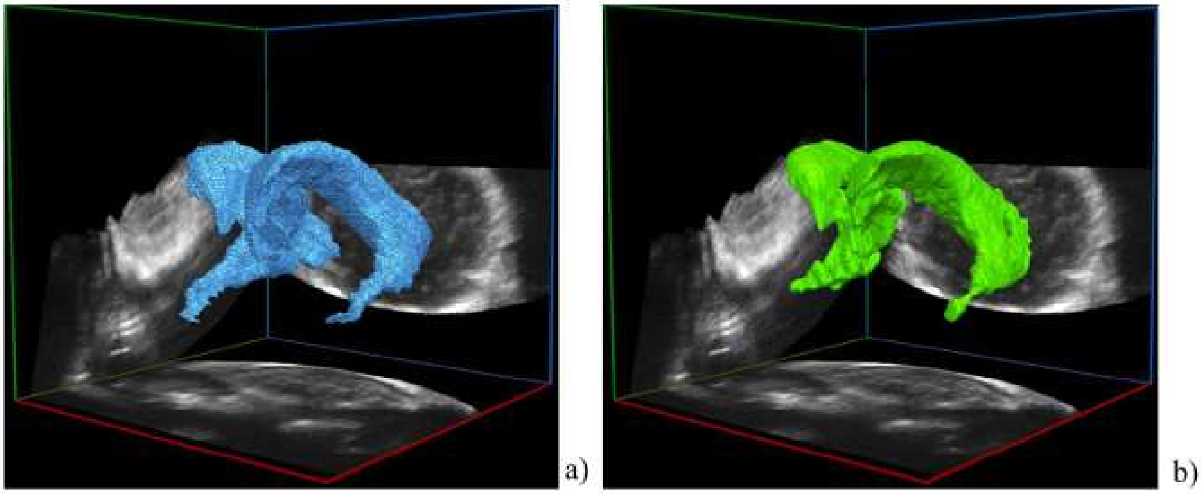

Figure 1. Manual a) and automatic b) segmentation of the cerebral ventricular system in a 3D reconstructed volume [Martin-18]