

5.0 DATA

The data used to test the hypothesis and aims introduced in the previous chapter are drawn from a set of simulated rs-fMRI sequences and four clinical groups. In this chapter, we will first discuss the mechanism built to simulate brain activity, scanner noise, and motion in rs-fMRI sequences. Then we will discuss the clinical images, which were taken from two studies: a prospective study of congenital heart defects in pediatric patients and a prospective study of Alzheimer’s disease in the aging population. Subjects from these two studies were chosen because patient motion causes problems in MR images across all stages of life, though patients may exhibit different types of motion at different stages of life.

5.1 SIMULATED SEQUENCES

There are two major barriers in medical imaging research. The first barrier is that it is difficult to obtain enough data from a large number of subjects to perform large-scale studies. The second barrier is the complexity of identifying a gold standard. Specifically, if the gold standard brain signal which motion correction techniques attempt to recover was known, there would be no need for image processing in the first place. We addressed these two barriers by creating a mechanism for generating a simulated image sequence which includes functional connectivity based brain activity, scanner noise, and simulated patient motion. Our mechanism can create large quantities of unique image sequences. The simulated image sequences can also serve as a gold standard for evaluating volume registration and motion correction techniques: the signals and noise sources added to the sequence are known with certainty.

5.1.1 SPECTr: Simulated Phantom Emulating Cranial Transformations

Our mechanism is called Simulated Phantom Emulating Cranial Transformations (SPECTr). A phantom is an object designed to have material properties which mimic those of a specific tissue type or organ. Phantoms, either manufactured or healthy human, are used in multicenter studies to obtain images of the same object or person from multiple scanners. These images are used to harmonize the data taken from the different sites. We call our simulated sequence a phantom because the baseline image itself is known as are the signals added to it to simulate brain activity and cranial motion.

The process for generating a simulated sequence using SPECTr has several steps and uses a known rs-fMRI sequence. First, a single image volume is selected from the known rs-fMRI sequence. A mask of this volume is created and will be used later in the SPECTr pipeline. The chosen volume is duplicated to create a sequence with N (default $N = 150$) instances of the same volume. This sequence is called the base phantom sequence.

Next, brain signal is added to the base phantom sequence. The location of the brain signals is limited to locations associated with the default mode network (CITATION). Information about healthy default mode networks are used to inform how much simulated BOLD signal could occur in different brain locations over time. In areas associated with healthy default mode networks, small signals are added. These signals are mixtures of 3D Gaussian distributions. Each distribution’s standard deviation and intensity scaling factor change between image volumes. These simulated BOLD signals are saved in a standalone simulated BOLD signal image file. They are also added to the base phantom sequence to create our BOLD phantom sequence. The BOLD phantom sequence serves as the ground truth for any motion correction pipeline: it contains the known brain orientation and BOLD signal independent from head motion and scanner noise.

Now that the ground truth brain orientation and BOLD signal have been established, patient motion can be added to the BOLD phantom sequence. First, a reasonable range of head rotation about the x-, y-, and z-axes was established. These angle ranges are used to generate rotational transformation matrices for $N - 1$ image volumes. The transformations are applied to each image volume after the first volume in the BOLD phantom sequence. The

transformed image sequence is referred to as the BOLD phantom sequence with motion and the rotational transformation matrices are saved as the ground truth for the transformations between each image volume and the template volume.

Finally, scanner noise is added to the BOLD phantom sequence with motion. As discussed in Chapter 2, there are several sources of scanner noise caused by combinations of electromagnetic signal changes in the magnetic field and tissue susceptibility due to patient motion. These noise sources are not addressed in this work, but are simulated as part of SPECTr’s pipeline. SPECTr models scanner noise as a randomly generated speckle pattern which is applied to each volume in the BOLD phantom sequence. The sequence containing simulated BOLD signal, patient motion, and scanner noise can now be used to evaluate the efficacy of motion correction pipelines in removing motion and scanner noise from rs-fMRI sequences.

5.1.2 Simulated Images

We used a healthy adult male rs-fMRI as the known rs-fMRI sequence for SPECTr and created 100 simulated sequences. The parameters for the BOLD signal, the head rotations, and the speckle patterns are as follows:

- **BOLD Signal**

- Standard deviation range: $[1, 5]$
- Signal scaling range: $[1, 5]$

- **Head Rotations (Patient Motion)**

- Rotation about z-axis (looking left and right): $[-75^\circ, 75^\circ]$ assuming looking left is a negative rotation and looking straight forward is 0°
- Rotation about y-axis (looking up and down): $[45^\circ, -20^\circ]$ assuming looking down is a negative rotation and looking straight forward is 0°
- Rotation about the x-axis (stretching neck by bringing left ear to left shoulder or right ear to right shoulder): $[-60^\circ, 60^\circ]$ assuming leaning right is a negative rotation and looking straight forward is 0°

- **Speckle Patterns (EM Scanner Noise)**

- Speckle variance: variance of the uniform distribution used to generate the speckle noise, uses the range [0.05, 1]

The source code for SPECTr is available on Github.

5.1.3 Purpose of Dataset

The phantom experiments are used to probe the volume registration techniques and the motion correction technique. By applying the DAG-based and traditional registration techniques to the base phantom sequence, we evaluate the degrees of positional and signal change errors each technique may introduce into the registration process. The registered versions of the BOLD phantom sequence are compared to each other and to the original BOLD phantom sequence to determine how well each registration retains the BOLD signal.

This particular experiment will be one of the first to investigate how much true BOLD signal is preserved through motion correction. One of the major drawbacks to existing motion correction pipelines is that they remove signal along with noise. In clinical data, there is no way to know the ground truth signal contained within the image; however, simulated phantom images have a de facto known ground truth signal. The design for this experiment can be used to evaluate how much BOLD signal is recovered by other motion correction pipelines, and how close the recovered signal is to the signal of interest.

5.2 CONGENITAL HEART DISEASE COHORTS

Congenital heart defects and congenital heart disease (CHD) both refer to defects in the heart or the vessels around the heart which formed during fetal development. Heart defects affect how blood moves into, through, and away from the heart. However, cardiac conditions are not the only complications CHD must deal with. In recent years, researchers have found that there is a relationship between CHD and neurocognitive disorders. The CHD rs-fMRIs used in this study were gathered as part of ongoing studies of the relationship between CHD and neurodevelopment. Data from these studies was obtained through studies approved by