

## Estimation of the arterial input function using accelerated dual-contrast EPIK: a multi-modality MR-PET study

Liliana Caldeira<sup>1</sup>, Seong Dae Yun<sup>1</sup>, Nuno A da Silva<sup>1</sup>, Christian Filss<sup>1</sup>, and N Jon Shah<sup>1,2</sup>

<sup>1</sup>Institute of Neuroscience and Medicine - 4, Research Centre Jülich GmbH, Jülich, Germany, <sup>2</sup>Department of Neurology, RWTH Aachen University, Aachen, Germany

**Target Audience:** Individuals interested in arterial input function and parametric imaging.

**Purpose:** The arterial input function (AIF) is essential for quantification in MRI and PET imaging. The AIF is a function that describes the arrival of contrast agent to the tissue of interest. The gold standard for AIF estimation is arterial cannulation, which is an invasive and laborious procedure. Alternatively, the AIF can be estimated using MRI and/or PET images. For an appropriate estimation of the AIF, a reasonable temporal resolution of dynamic image series is necessary (<2s). In PET imaging, minimum frame length is usually 5s, while in MRI, higher temporal resolution can be achieved for AIF estimation. For accurate AIF localization (e.g. carotid artery) and for posterior calculation of brain perfusion maps, it is necessary to have a reasonable spatial resolution ( $1.875 \times 1.875 \times 5 \text{ mm}^3$ ) and spatial coverage ( $230 \times 230 \times 135 \text{ mm}^3$ ) of the whole brain, respectively. For this purpose, the present work uses the accelerated EPI with keyhole (EPIK)<sup>1,2</sup> scheme for the MRI acquisition, which has been validated to have a sufficient capability for the addressed conditions. Here, the accelerated EPIK scheme was further extended to a dual-contrast version<sup>3</sup> to exploit the dual contrast information in the AIF estimation. The proposed method is demonstrated with an *in vivo* measurement where Gd-DTPA contrast injection was applied.

**Methods:** For this work, a Siemens (Erlangen, Germany) hybrid 3T MR-BrainPET scanner with an 8-channel phased array coil from the manufacturer was used. A simultaneous brain MR-PET acquisition was performed on a male volunteer. The PET tracer was injected while the patient was inside the scanner and thus the AIF can be estimated. PET data were acquired in list-mode format, which can then be sorted into appropriate frames. PET images were reconstructed with the following 23 frames using standard reconstruction protocol: 8x5s, 4x10s, 1x45s, 2x90s, 1x180s, 4x300s and 3x600s. All PET corrections were taken into account: normalisation, randoms, scatter and attenuation. Gd-DTPA was administered to the patient with a power injector (Injektron 82 MRT Medtron AG) while the EPIK sequence was running. The MR data were acquired using the two-fold dual-contrast (DC) EPIK. Figure 1a shows a three-shot EPIK scheme where the top k-space lines are skipped for a later partial Fourier reconstruction. Each measurement scans the central k-space region (keyhole region:  $K_k$ ) completely with  $\Delta k_y = 1/\text{FOV}$ , whilst the peripheral k-space regions (sparse region:  $K_s$ ) are sparsely sampled with  $\Delta k_y' = 3/\text{FOV}$  resembling a three-shot EPI scheme. By sharing the sparse region data from three consecutive scans with the keyhole region updated for every measurement, one obtains an image per TR excluding 2 initial dummy runs, where the top missing lines are computed from the projection onto convex sets (POCS) algorithm<sup>4</sup>. The acquisition scheme is further accelerated with a parallel MRI acceleration factor of two (see Fig. 1b), resulting in a two-fold EPIK. This example features one-fourth of k-space as the keyhole region, resulting in the total number of phase encoding lines reduced to 3/16 of a comparable EPI sequence. In a time-series of images, the fourth acquisition replaces the data from the first in a sliding window fashion. In this way, the two-fold EPIK is repeated twice per TR to acquire dual contrasts defined by  $TE_1$  and  $TE_2$ , which may help to establish a diagnosis in a clinical setting by providing more parametric images<sup>5</sup>. The MR data were acquired using the two-fold dual-contrast (DC) EPIK with the following parameters:  $\text{FOV} = 240 \times 240 \text{ mm}^2$ , matrix size =  $128 \times 128$ ,  $\text{TR}/\text{TE}_1/\text{TE}_2 = 1000/12/70 \text{ ms}$ , slice thickness = 5 mm with 8 slices and 100 temporal volumes. When a minimum TE was used, the minimum TR computed from the two-fold DC-EPIK was 64.53 ms which was even smaller than that of a comparable two-fold EPI case (73.29 ms). The proposed acquisition provides a unique framework to study AIF estimation methods using PET and MRI images for human studies. It has been shown in the literature that AIF obtained with PET and MR data have similar features and can be converted into one another<sup>6</sup>. Moreover, there are several possibilities to model the AIF, but we used a gamma-function fitting as this is the most common fitting for MRI signals.

**Results:** In this work, the method was first demonstrated with a resolution phantom to assess image quality. Then, three subjects (without Gd-DTPA contrast) were measured to assure appropriate image contrasts in brain tissues using the proposed sequences. Finally, a patient data were acquired with  $^{18}\text{F}$ -FET (274 MBq) and Gd-DTPA (0.1 mmol/Kg body weight). Figure 2a shows the reconstructed images from the patient data obtained at the 10-th temporal scan. In Fig. 2a, the two left images and the two right images show the very same reconstructed slice from the first and second echo data, respectively. Compared to these images, a substantial decrease of signals is observed at the 30-th scan (see Fig. 2b) due to the Gd-DTP-induced contrast change. From the entire temporal scans, the AIF functions were estimated separately from the first and second echo data as shown in Fig. 2c.

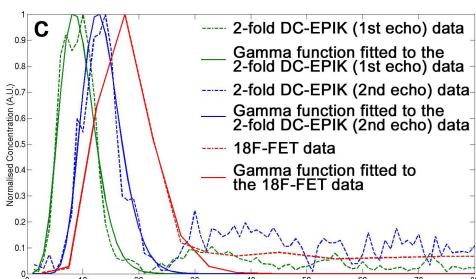
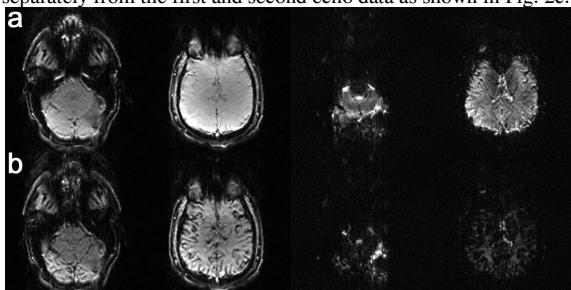


Figure 2. Reconstructed MR images at the (a) 10-th and (b) 30-th temporal scans. In each row, the two left and two right images were obtained from the 1st and 2nd echo data, respectively. (c) AIF obtained from the carotid and venous region with DC-EPIK ( $AIF(t) = 1/TE^*S(t)/S_{\text{baseline}}$ ) and  $^{18}\text{F}$ -FET (curves normalized to the maximum of each curve, which was different for each curve). Curves are shown from 10 seconds after injection.

**Discussion:** The estimated AIF from each contrast data had a similar shape to the one from the  $^{18}\text{F}$ -FET data. However, one should mention that both DC-EPIK and  $^{18}\text{F}$ -FET have not been corrected for partial volume effect, delay and dispersion (additional invasive procedure is required) and therefore, the shape of curves might be slightly affected. Moreover, there is still activity in the carotid after 40s in the  $^{18}\text{F}$ -FET curve (as seen in previous studies in our Centre), which means that functions other than the gamma-function could be more appropriate (e.g. sum of exponentials). Furthermore, the two-fold DC-EPIK allows the acquisition of dual-contrast information in a similar acquisition time of a comparable two-fold EPI, thus the accelerated DC-EPIK method is of great interest for characterisation of the AIF.

**Conclusion:** In this work, we have demonstrated the acquisition of a dynamic MRI series with the two-fold DC-EPIK. The obtained dynamic MRI series allowed estimation of the AIF with a high temporal resolution of 1s, which had a similar shape to the one from the  $^{18}\text{F}$ -FET data.

**References:** 1. Zaitsev M, Zilles K, Shah NJ. Magn Reson Med. 2001;45(1):109-17. 2. Yun S, Reske M, Vahedipour K, et al. Neuroimage 2013;73:135-143. 3. Zaitsev M, Arcy JD, Collins DJ, et al. Phys Med Biol 2005;50:4491-4505. 4. Haacke EM, Brown RW, Thompson MR, et al. Magnetic resonance imaging: physical principles and sequence design, 1999, New York: Wiley. 5. Barbier EL, Lammale L, Décorps M. Journal of Magnetic Resonance Imaging 2001;13(4):496-520. 6. Poulin E, Croteau E, Blanchette M, et al. Magnetic Resonance in Medicine 2013;69(3):781-792.