4D-CT Simulation using Individually Optimized Contrast Enhancement (CE): A Phantom Study

**Innovation/Impact:**
4D-CT simulation has been widely used to estimate the respiratory motion of lung tumors and abdominal tumors for radiotherapy planning. However, most abdominal tumors (liver, pancreas etc.) cannot be readily visualized in CT without dynamic CE. It is desirable to combine a 4D-CT without CE and a CE 3D-CT into a CE 4D-CT so that we can both visualize the tumor and estimate its motion in a single scan. Due to the very long scan time of 4D-CT (60-75 s), it is impossible to have peak CE present throughout the entire scan, therefore, one has to set a delay time between the injection of the contrast medium and the start of 4D-CT so that the CE is maximized when scanning the tumor region. In previous studies, the delay time has been set to scan the central part of the tumor at a fixed time from the injection (“A.S. Bedder, 2008, P. Mancosu, 2008”). Such fixed-timing methods did not take into consideration of the large variation in the peak CE time from one patient to another (e.g., 19 – 48 sec for the pancreatic phase, see “L. van Hoe, 1995”) and thus are not optimal for all patients. We propose to use test injection to optimize the delay time in CE 4D-CT for individual patients. To our knowledge, this is the first such study in 4D-CT. In this work, we designed a phantom and demonstrated the feasibility of individually optimizing the delay time in CE 4D-CT.

**Materials and Methods**

**Phantom:** We use a fiber dialyzer filled with water (Fig. 1) to simulate an organ of interest. A dual-head power injector (Stellant, Medrad, Pittsburgh, PA) is used to inject contrast medium into the top opening of the dialyzer. The contrast medium flows from the top to the bottom and exits through the bottom opening of the dialyzer, simulating the dynamic contrast enhancement and washing out in an organ.

**CE 4D-CT scan protocol:** We performed this study on a 16-slice Brilliance Big Bore CT scanner (Philips Healthcare, Andover, MA). Firstly, we measured the length, L₀, from the starting position of the 4D-CT scan to the center of the phantom or organ on a surview scan as illustrated in Fig. 2. Secondly, we performed a series of axial scans with test injection at the center of the phantom to measure the peak CE time for the test injection (T*peak,test*). We then estimated the peak CE time (T*peak*) and the optimal delay time between the injection of the full contrast medium and the start of 4D-CT (TIV), as explained below. Finally we initiated a 4D-CT scan and started contrast injection after TIV. The parameters for the 4D-CT scan were: collimation 16×1.5 mm (24 mm), pitch 0.071, and gantry rotation time 0.5 s, resulting in a table speed of V=3.408 mm/s.

**Contrast injection protocol:** We use 30 mg/mL iodine contrast (diluted from Omnipaque-300, GE Health Care, Princeton, NJ). To simulate blood washing and saline flushing in patient study, we injected distilled water into the phantom immediately following contrast injection. The injection rate was set at 3 mL/s. In test injection, a small bolus of 10 mL contrast was injected, followed by 60 mL water. In full bolus injection for the CE 4D-CT, 140 mL contrast was injected followed by 120 mL of water. The time it takes for 4D-CT to reach the center of the phantom T₀ = L₀/V was longer than the peak CE time T*peak*. Therefore, an injection delay time, TIV = T₀ − Tpeak (Eq. 1) is programmed on the power injector so that the CE is maximized at the center of the phantom.

**Estimation of the peak CE time T*peak*:** The contrast enhancement pattern of the phantom agreed well to a linear model (see Results section). If we denote Tarr as the contrast arrival time, Tpeak,test and Tpeak as the peak CE times of the test bolus and full bolus injections, respectively, and TD,test and TD as the corresponding injection durations, from the following equations T*peak,test = Tarr + TD,test and T*peak = Tarr + TD, we can estimate T*peak from T*peak,test as: T*peak = T*peak,test − TD,test + TD (Eq. 2). By using an injection delay time TIV = T₀ − Tpeak (Eq. 1), maximum CE occurs at the center of the phantom.
Results
To test the reproducibility of the contrast enhancement curves, we performed three repeated axial scans for both test injection and full-bolus injection at the central slice of the dialyzer, using 60 mg/mL contrast. The measured $T_{arr}$, $T_{peak}$, the peak CT number $CT_{peak}$, and the estimated peak time $T_{peak}^{test}$ are summarized in Table 1. We notice that the estimated $T_{peak}$ is quite close to the measured $T_{peak}$, with a mean error of -0.4 s. The peak CT number $CT_{peak}$ is very stable (734±8 HU). This accurate estimation of $T_{peak}$ from $T_{peak}^{test}$ and the stability of $CT_{peak}$ enable us to further test the CE 4D-CT.

To better simulate the degree of CE in patients (250-350 HU), we reduced the contrast medium concentration to 30 mg/mL in all following studies. Typical contrast enhancement curves from axial scans of both test injection and full bolus injection are shown in Fig. 3. The enhancement curves are very similar to those from the patient studies.

We then performed five CE 4D-CTs with test injection to verify that our CE 4D-CT scan protocol actually catches the maximal CE of the phantom. The setup parameters are the same in these five scans: $L_0$=270 mm ($T_0$=79.2 s), $T_{ID}^{test}$ = 3.3 s, $T_{ID}$ = 46.7 s, which resulted in: $T_{peak} = T_{peak}^{test}$ + 43.3 s, and $T_{IV} = T_0-T_{peak} = 35.9$ s – $T_{peak}^{test}$. In these five trials, we intentionally applied five different additional delays ($\Delta T$) of +6, +3, 0, -3 and -6 s, to the estimated optimal injection delay time $T_{IV}$. Therefore, the actual delay time was $T_{IV} = T_{IV} + \Delta T$ (see Table 2). The average contrast enhancement (in HU) of a 1.5 cm$^3$ VOI that centered at the ROI of the phantom is measured in each 4D-CT, using a 3D-CT without contrast as baseline. We noticed that the 4D-CT using the optimal $T_{IV}$ ($\Delta T = 0$) showed the maximum contrast enhancement (Table 2 and Figure 3). The larger deviations ($\Delta T$) resulted in the lower contrast enhancement. These results verified that the estimated optimal injection time delay achieved maximum contrast enhancement at the center of the phantom.

Conclusions
Based on the phantom study, we conclude that it is feasible to estimate individually optimized injection delay time to maximally enhance a region or organ of interest in CE 4D-CT.