Dual phase cone beam CT as a tool to appreciate the micro-embolic effect of radioembolization

Poster No.: C-0311
Congress: ECR 2012
Type: Scientific Paper
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Keywords: Interventional vascular, Oncology, Liver, Catheter arteriography, CT-High Resolution, Radioembolisation, Embolisation, Metastases
DOI: 10.1594/ecr2012/C-0311

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Purpose

Radioembolization, performed with TheraSpheres® (MDS Nordion, Ottawa, Ontario, Canada) is an interventional oncology technique for treating liver tumors. The uniqueness of TheraSpheres® is the small size and amount of embolic material used (20 to 30 µm diameter, average of 1.2 million beads). As such, the radioactive spheres can be carried closer to the tumor and produce microscopic embolization at the tumor capillary bed while not affecting flow in the intra-hepatic arterial branches. The spatial resolution of modern x-ray digital subtraction angiography (DSA) systems is insufficient to resolve any signal modification at the tumor level because the TheraSpheres® are so small. C-arm cone-beam computed tomographic (CBCT) technology has emerged as a useful tool in conjunction with standard DSA for the treatment of liver tumors. In addition to having a higher contrast resolution as compared to DSA (contrast resolution 1 to 10 HU), CBCT generates a 3D image that does not suffer from superimposition.

CBCT can also provide additional information about tumor and tissue perfusion. For example, CBCT is equally as sensitive as multiphasic MRI in detecting tumors. A recent improvement of the CBCT is Dual-Phase CBCT (DPCBCT). DPCBCT (Philips Healthcare, Best, The Netherlands) can acquire multi-phasic scans using only one injection of contrast media. When used for radioembolization, DPCBCT captures two enhancement phases of the same hepatic-tumor structure. The early arterial phase shows the normal arterial network and the abnormal tumor neo-vessel network. The delayed phase shows tumor enhancement at the capillary level.

The purpose of our study was: 1) to evaluate micro-embolic effect induced by TheraSpheres® at the capillary level by comparing delayed phase tumor image enhancement before and after radioembolization. 2) To determine whether TheraSpheres® induce macrovascular flow reduction or occlusion (at the level of the hepatic arteries) by comparing early arterial DPCBCT images before and after radioembolization.

Methods and Materials

Patient selection

This was a single-institution prospective trial, in which all imaging was analyzed retrospectively. It was compliant with the Health Insurance Portability and Accountability Act (HIPAA) and was approved by the Institutional Review Board (IRB). All patients provided informed consent before inclusion in the study.

Radioembolization procedure:
Radioembolization was performed with TheraSpheres®. Regardless of the tumor burden, all patients had single lobar treatments. For bilobar presentation, treatment was split into two separate sessions, approximately 30 days apart. No whole-liver administration was performed. Lobar treatment was targeted to deliver an absorbed dose of 120 Gy according to previously published dosimetry techniques.

Dual-Phase CBCT data acquisition (Figure 1)

All patients underwent C-arm dual-phase CBCT imaging prior to and immediately after radioembolization. Imaging was performed using a commercially available angiographic system (Allura Xper FD20, Philips Healthcare, Best, The Netherlands). This system was equipped with the XperCT option, enabling C-arm CBCT acquisition and volumetric image reconstruction (Feldkamp back projection). For each CBCT scan, the region of interest was positioned in the system iso-center, and over approximately 10 seconds, 312 projection images (30 frames per second) were acquired with the motorized C-arm covering a 220° clockwise arc. As the images were acquired, the projections were reconstructed to produce volumetric data. The two-dimensional projection images were reconstructed using Feldkamp back projection into 3D volumetric images with 0.98 mm isotropic resolution for a 250 × 250 × 194 mm field of view (FOV) (matrix size 256 × 256 × 198) (14). The DPCBCT feature allows the acquisition of two sequential, back-to-back CBCT scans so both early and delayed arterial phases are captured using only one contrast injection (12). In this study, the two scans were triggered at 3 and 28 sec following a selective single injection of undiluted contrast medium through a 3-French co-axial microcatheter (Renegade® HI-FLO™, Boston Scientific, Natick, MA USA) placed into the proper hepatic artery. The same contrast injection protocol was applied to all cases (amount, 20 mL; rate, 2 mL/sec; Oxilan 300 mg I/mL, Guerbet, Roissy France). The patients were instructed to be at end-expiration apnea during each of the CBCT scans with free breathing between the early and delayed scans. Oxygen was administered to patients during the procedure to minimize the discomfort of breath holding. One millimeter-thick CT-like axial images were obtained for analysis.

Image Analysis

Two experienced Interventional Radiologists evaluated all DPCBCT images using ImageJ software (National Institutes of Health, Bethesda, MD, USA). This software was used to calculate the image intensity level of a target structure. Region of Interests (ROIs) were drawn on one axial slice for each phase of DPCBCT before and after radioembolization. For each DPCBCT, the signal intensity (mean, standard deviation, and range value) of liver tumor, right lumbar muscle, right retro-peritoneal fat, and non-enhanced healthy liver were measured. The intensity measurements in muscle, fat, and non-enhanced healthy liver pre-/post-radioembolization and at both DPCBCT phases were considered as a signal base reference. The signal intensity of the tumor was then measured using the same axial slice pre-/post radiation and same sized ROI (Figure
2). To mitigate any signal intensity modification, the same window level and width were applied to all four data groups (early and delayed scans for pre-/post-radioembolization). Image artifacts were defined as the presence of streak artifacts and/or motion artifacts and/or artifacts from the catheter placed in the hepatic artery.

Images for this section:
Fig. 1: Representative view of the Dual-Phase CBCT concept. Imaging is performed using a commercially available angiographic system (Allura Xper FD20, Philips Healthcare, Best, The Netherlands) equipped with the XperCT option, enabling C-arm CBCT acquisition and volumetric image reconstruction (Feldkamp back projection). For each CBCT scan, the region of interest is covered by 312 projection images (30 frames per second) covering a 220° clockwise arc. As the images are acquired, the projections
are reconstructed to produce volumetric data with 0.98 mm isotropic resolution for a 250 \times 250 \times 194 \text{ mm} \text{ field of view (FOV)} (\text{matrix size} 256 \times 256 \times 198) (24). The DPCBCT feature allows the acquisition of two sequential, back-to-back CBCT scans so both early and delayed arterial phases are captured using only one contrast injection. In this study, the two scans were triggered at 3 and 28 sec following a selective single injection of undiluted contrast medium through a 3-French co-axial microcatheter placed into the proper hepatic artery.
Results

Between January 2011 and July 2011, 14 consecutive patients (11 men, 3 women; mean age, 66 years; ± 7.1 [range 53 - 78]) who had radioembolization performed for carcinoid and neuroendocrine hepatic-dominant malignancies were included in this study. All patients underwent DPCBCT scans before and after radioembolization.

Seventy-two tumors were studied (average tumor per patient: 5.14 tumors ± 3.3 [Range 1 - 13]). The mean tumor diameter was 44 mm ± 19.36 [Range 12 - 88]. A total of 456 signal intensity measurements were performed for the 72 tumors including 14 right lumbar muscle ROIs, 14 right retro-peritoneal fat ROIs, and 14 non-enhanced healthy liver ROIs. This included all pre- and post-radioembolization for both early and delayed arterial phases of DPCBCT.

Table 1: Image intensity level results before and after radioembolization procedure, at early and delayed arterial dual phase cone-beam CT phases. And difference of image intensity level between pre- and post-radioembolization at early and delayed arterial phases, grouped by ROI. Values Mean ± standard deviation [range], AU - Arbitrary Units.

A high image intensity difference (1050 AU) with strong statistical significance (p-value < 0.001) was observed in the tumor in the delayed arterial phase between the pre- and post-radioembolization. Though a statistical difference (p-value < 0.001) was also observed in the tumor for the early arterial phase between pre- and post-radioembolization, the image intensity difference was lower than that of the delayed phase (183 AU vs. 1050 AU).

No statistical significance difference was noted for the right lumbar muscle, right retro-peritoneal fat, and non-enhancing healthy liver for both phases, before and after radioembolization. A representative patient case is presented in figure 2. Note the similar level of tumor enhancement between the pre-/post-Y90 early arterial phase (Figure2) and the significant level of enhancement difference for the delayed phase.

Images for this section:
Fig. 2: Representative Dual-phase CBCT images (in 3 mm thick MIP* post processing), of the early and delayed arterial phase before radioembolization procedure (a & b), and early and delayed arterial phases after procedure (c & d). A region of interest (ROI) was drawn on tumor and surrounding hepatic tissue. Same size ROI at the same slice level, with the same widow level for all slice reading. Here, the ROI size was 1232 pixels. The image intensity values measured were fig.2a 18578.02 arbitrary units (AU); fig.2b 18355 AU, fig.2c 18325 AU, and fig.2d 17521 AU. The results between pre-/post-Y90 delayed phase (figure 2b & d) show a significant tumor intensity level decrease (from 18355 to 17521 AU) after radioembolization procedure, a consequence of the micro-embolic effect. * MIP was used for visualization purposes. Image analysis was done using thin slice.
### Table 1: Image intensity level results before and after radioembolization procedure, at early and delayed arterial dual phase cone-beam CT phases. And difference of image intensity level between pre- and post-radioembolization at early and delayed arterial phases, grouped by ROI. Values Mean ± standard deviation [range], AU - Arbitrary Units

<table>
<thead>
<tr>
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<th>Pre-radioembolization</th>
<th>Post-radioembolization</th>
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<td><strong>Early Arterial Phase</strong></td>
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<tr>
<td>Tumor n=72</td>
<td>20340.7±1459.5 [18103.5, 25195.4]</td>
<td>20158.2±1416.6 [18230.8, 25003.8]</td>
<td>&lt;0.001</td>
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<td>Muscle n=14</td>
<td>18880.3±1563.7 [16518.8, 22179.8]</td>
<td>18866.8±1611.2 [16622.0, 22226.1]</td>
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<td>Fat n=14</td>
<td>16631.0±1380.3 [14428.1, 19394.6]</td>
<td>16610.8±1314.5 [14559.1, 19619.9]</td>
<td>0.78</td>
</tr>
<tr>
<td>Healthy Liver n=14</td>
<td>18474.5±965.6 [16966.6, 21184.4]</td>
<td>18381.9±960.2 [16996.1, 20951.7]</td>
<td>0.03</td>
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<tr>
<td><strong>Delayed Arterial Phase</strong></td>
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<tr>
<td>Tumor n=72</td>
<td>20091.4±963.6 [18469.6, 23271.9]</td>
<td>19040.7±981.2 [16554.1, 21742.7]</td>
<td>&lt;0.001</td>
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<tr>
<td>Muscle n=14</td>
<td>18637.6±1719.1 [16549.5, 23202.9]</td>
<td>18616.7±1760.3 [16604.0, 23426.1]</td>
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<tr>
<td>Fat n=14</td>
<td>16628.5±1078.9 [15210.4, 19014.4]</td>
<td>16557.3±1120.2 [15068.2, 18902.0]</td>
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<tr>
<td>Healthy Liver n=14</td>
<td>18431.0±1247.7 [16840.2, 22184.5]</td>
<td>18297.5±1307.7 [16910.3, 22142.7]</td>
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<tr>
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<th>Early Arterial Phase</th>
<th>Delayed Arterial Phase</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Tumor</td>
<td>182.5±190.9 [217.6, 792.8]</td>
<td>1050.6±213.1 [396.0, 4125.5]</td>
<td>&lt;0.001</td>
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<td>Muscle</td>
<td>13.5±192.1 [280.5, 372.5]</td>
<td>20.8±163.6 [258.7, 198.7]</td>
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<tr>
<td>Fat</td>
<td>20.1±269.9 [382.6, 542.5]</td>
<td>71.2±154.1 [179.8, 252.2]</td>
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Conclusion

Tumor imaging at both early (tumor feeding vessel enhancement) and delayed arterial (tumor parenchymal enhancement) phases using only one intra-arterial injection of contrast medium is possible using DPCBCT. DPCBCT’s ability to assess 3D perfusion changes related to transarterial embolization demonstrate that radioembolization causes 1) a micro-embolic effect at the capillary level, and 2) no macro-embolic effect on tumor feeding arteries. This intra-procedural imaging concept appears as a promising technical development with numerous clinical ramifications, especially with other embolization procedures.

References


Personal Information