64-MDCT perfusion of the esophageal cancer using the deconvolution-based commercial software: comparison with the maximum slope analysis and the standardized perfusion value

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**Purpose**

1. To compare the 64-MDCT perfusion measurements of the blood flow and blood volume of the esophageal carcinoma, using the deconvolution-based software, with the corresponding perfusion values calculated according to the maximum slope methodology at the same tumor volume samples and to estimate if those values are in agreement, or at least interchangeable.

2. To assess the correlation between the SPV, which is proposed to be a universal semi-quantitative indicator of tumor perfusion, and the corresponding quantitative perfusion measurements: tumor blood flow and tumor blood volume, obtained by two different kinetic CT perfusion models.
Methods and Materials

Participants

- Thirty-one consecutive patients (27 men, 4 women; mean age 62; range, 44-75 years) with the endoscopic biopsy-proved carcinoma of the esophagus were enrolled in this prospective study.

- CT perfusion study was incorporated in the conventional CT examination of patients with the esophageal cancer, on the basis of pretreatment staging.

- Institutional Ethics Board approved this study, and written informed consent was obtained from each subject.

- Twenty-six esophageal tumors were squamous cell carcinomas and five were adenocarcinomas.

- According to the CT criteria of staging, two patients had T2, 22 had T3, and seven had T4 neoplasm.

- Tumors were located in both the cervical and upper thoracic portion of the esophagus in one patient, the upper thoracic portion in 4, the upper and middle thoracic portion in 3, the midthoracic portion in 10, the middle and lower thoracic portion in 4, the lower thoracic portion in 3, and the lower esophagus and cardia in 6 patients.

- Mean length of tumors, assessed by measuring on computed tomography, was 6.87 ± 2.18 cm (range, 3-12 cm).

Perfusion CT scans

- CT was performed with the 64-detector row CT (LightSpeed VCT, GE Health-care Technologies).

- First series was an unenhanced low-dose thoracic CT scan, which was performed to identify the tumor and plan the CT perfusion study, was restricted to the expected region of tumor extension (axial-mode, 5 mm-section thickness, 1-s rotation time, detector coverage 40 mm: 8 images per rotation, 80 kV, 40 mAs, 25-cm scan field of view, 16-24 slices, 2-3 s total exposure time). This series was viewed, and, after identification of the
tumor as localized segmental esophageal wall thickening, eight contagious sections at the level of the greatest tumor area were chosen for the following perfusion study and spatial coordinates were recorded.

- Second series was a low-dose CT perfusion study. For the perfusion CT study, 50 ml of the non-ionic iodinated contrast (370 mg/ml of iodine), followed by 30 ml of saline, was administrated intravenously using the pump injector (Urlich-Missuri, Urlich, Germany), at a flow rate of 7 ml/s, through a 16-gauge cannula that was placed in the ante-cubital vein. Using the cine-mode acquisition, eight contagious sections, with 5-mm axial thickness (totally 40 mm z-axis coverage), which were previously chosen in the unenhanced series, were scanned at 1-second intervals (80 kV, 40 mAs, 25-cm scan field of view, 512 x 512 matrix) (Fig. 1 on page 6). Scanning started 5 seconds after the beginning of the intravenous contrast administration, and total scan duration was 50 seconds (400 images per a study). Patients were advised to breathe quietly during the dynamic CT scanning.

- Third series was a conventional portal venous phase CT of the neck, thorax and the abdomen, after the intravenous administration of 60-100 ml iodinated contrast, performed for the staging purposes.

**Imaging data analysis**

- All CT series were transferred to the workstation (Advantage Windows 4.3, GE Healthcare Technologies) and analyzed by one radiologist (corresponding author, fourteen years of experience in the thoracic-abdominal radiology and five years in the perfusion CT).

- CT perfusion series were analyzed with the commercial deconvolution-based perfusion software (Perfusion 3.0, GE Healthcare Technologies).

- Arterial input was defined by the circular region of interest (ROI), area of which was 4-6 mm$^2$ that was placed in the center of the descending aorta, aortic arch, or common carotid artery, depending on the esophageal neoplasm localization. Then, the arterial time-density curve was derived automatically, and parametric colored maps were computed for each of eight contagious series of the perfusion CT. Freehand ROIs were drawn around the tumor margins at the reference and parametric images on each of eight contagious slices, taking care to avoid the esophageal lumen if it was visible, areas of the tumor necrosis and periesophageal fat (Fig. 2 on page 6). Thus, the tumor time-density curves were displayed together with previously derived arterial time-density curve at the same coordinate system for each of eight contagious slices (Fig. 3 on page 7).
- Values of the automatically calculated and displayed tumor BF\textsubscript{deconvolution} (Fig. 4 on page 8) and BV\textsubscript{deconvolution} (Fig. 5 on page 9) were recorded for each section esophageal tumor ROI.

- Values of the tumor blood flow- F\textsubscript{ms} (ml/min/100 g tissue), and blood volume- V\textsubscript{ms} (ml/100 g tissue), for the same tumor ROIs, were calculated from the data displayed on the arterial and tumor time-density curves, using the maximum slope approach (Fig. 3 on page 7) [1,2, 3].

- Standardized perfusion values (SPV) were calculated for the same tumor ROIs, according to the methodology proposed by Miles K et al (Fig. 3 on page 7) [4]. For this purpose, body weight of each patient was recorded.

- At each section of each CT perfusion study, for the same tumor ROI, the mean values of the BF\textsubscript{deconvolution} (Fig. 4 on page 8), and BV\textsubscript{deconvolution} (Fig. 5 on page 9), which were automatically calculated by the commercial deconvolution-based CT perfusion software and displayed by the colored parametric perfusion maps were compared with F\textsubscript{ms}, and V\textsubscript{ms}, which were manually calculated from the arterial and tumor time-density curves, using the maximum slope methodology (Fig. 3 on page 7).

- In addition, the value of the SPV, calculated for the same tumor ROI (Fig. 3 on page 7), was correlated with the corresponding blood flow and blood volume perfusion measurements obtained by two different pharmacokinetic CT perfusion models.

**Statistical analysis**

- Shapiro-Wilk test was performed for assessing the normal distribution of the perfusion measurements.

- Wilcoxon matched-pairs test (Z), and Bland-Altman plots (25) were used to compare the perfusion measurements, and Spearman’s rank correlation coefficient ($r_S$) or Pearson’s linear correlation coefficient ($r$) to assess their correlations.
**Fig. 1:** An image from the low-dose CT perfusion series (second section in the cranial-caudal direction, 35th second of cine-scanning), of a patient with cancer of the middle esophageal portion (a freehand ROI in the region of tumor).

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Fig. 2: The reference image of the corresponding CT perfusion section: freehand ROI that was drawn around the tumor margins.

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Fig. 3: The tumor (green), and arterial (violet), time-density curves of the corresponding CT perfusion section (PAE: 670 HU; TTParterial: 14 s; PTE: 42 HU; TTPtumor: 16s;). Fms of 22.39 ml/min/100 g, Vms of 5.97 ml/100 g and SPV of 4.45 (mass of patient was 66 kg) were calculated [2,3,4].

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Fig. 4: Color parametric map of the tumor ROI's blood flow, automatically computed by the commercial CT perfusion software using the deconvolution method for the corresponding CT perfusion section (BFdeconvolution: 61.21 ml/min/100 g).

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Fig. 5: Color parametric map of the tumor ROI's blood volume, automatically computed by the commercial CT perfusion software using the deconvolution method for the corresponding CT perfusion section (BVdeconvolution: 4.14 ml/100 g).

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Results

Values of the perfusion measurements

- A total of 248 sections of the 31 CT perfusion studies were analyzed (31 pts × 8 slices per each CT perfusion study), and esophageal tumor was visible on 246 slices.

- "Slice-by-slice" and average "whole covered tumor volume" analysis of the selected perfusion parameter values was performed.

- Median values of the $BF_{\text{deconvolution}}$, and $F_{\text{ms}}$ obtained by "slice-by-slice" analysis (246 slices) were as follows: $75.10 \text{ ml/min/100 g}$ (range, 22.10-230.50), and $26.05 \text{ ml/min/100 g}$ (range, 7.13-96.41).

- Median values of the $BV_{\text{deconvolution}}$, and $V_{\text{ms}}$ were $5.85 \text{ ml/100 g}$ (range, 2.30-12.80), and $9.42 \text{ ml/100 g}$ (range, 3.44-19.40), respectively.

- Median value of the $SPV$ was $6.88$ (range, 2.08-16.22).

- Wilcoxon matched-pairs test revealed significant difference between both pairs of the perfusion measurements: $BF_{\text{deconvolution}}$ versus $F_{\text{ms}}$ ($Z=-13.523, p<0.001$), and $BV_{\text{deconvolution}}$ vs. $V_{\text{ms}}$ ($Z=-13.117, p<0.001$), respectively.

Agreement between the corresponding deconvolution and maximum slope perfusion measurements

- Mean differences and 95% limits of agreement between the blood flow, and blood volume values obtained by two different CT perfusion algorithms are presented using the Bland-Altman plots (Fig. 7 on page 13), (Fig. 9 on page 13).

- Poor agreement between both pairs of perfusion parameters is obvious, with clear bias that $BF_{\text{deconvolution}}$ values tend to exceed the $F_{\text{ms}}$, while the $BV_{\text{deconvolution}}$ values tend to decline the $V_{\text{ms}}$ (Fig. 6 on page 14), (Fig. 7 on page 13), (Fig. 8 on page 15), (Fig. 9 on page 13).
Correlation between the perfusion measurements and SPV

- Correlation between the SPV, and blood flow, so as the blood volume measurements obtained with two different algorithms, was analyzed (Table 2).

**Table 2** Correlation of the SPV with the blood flow and blood volume measurements obtained with the deconvolution and maximum-slope CT perfusion algorithms ("slice-by-slice" and "whole covered tumor volume" analysis)

<table>
<thead>
<tr>
<th></th>
<th>Slice-by-slice analysis (n=246)</th>
<th>Averages of the whole covered tumor volumes (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rs</td>
<td>p</td>
</tr>
<tr>
<td>SPV vs. BF&lt;sub&gt;deconvolution&lt;/sub&gt;</td>
<td>0.446**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SPV vs. F&lt;sub&gt;ms&lt;/sub&gt;</td>
<td>0.674**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SPV vs. BV&lt;sub&gt;deconvolution&lt;/sub&gt;</td>
<td>0.592**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SPV vs. V&lt;sub&gt;ms&lt;/sub&gt;</td>
<td>0.759**</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

rs: Spearman's rank correlation coefficient

r: Pearson's linear correlation coefficient

**: p<0.01
**Fig. 7:** Bland-Altman agreement plot of the difference between the BFdeconvolution (BF) and Fms (F), against their mean values (0: line of perfect agreement; thick continuous line in the middle: the mean difference; outer lines: 95% limits of agreement).

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**Fig. 9:** Bland-Altman agreement plot of the difference between the BVdeconvolution (BV) and Vms (V), against their mean values (0: line of perfect agreement; thick continuous line in the middle: the mean difference; outer continuous lines: 95% limits of agreement).

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Fig. 6: BFdeconvolution versus Fms agreement diagram: the majority of data points lie above the line of equality (y=x).

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Fig. 8: BVdeconvolution versus Vms agreement diagram: the majority of data points lie below the line of equality (y=x).

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Conclusion

- Tumor blood flow and blood volume measurements obtained with the deconvolution-based and maximum slope CT perfusion analysis do not agree between each other and consequently are not interchangeable.

- Generally, significantly higher values of the blood flow (on average 2.8 times), and lower values of the blood volume (on average 1.7 times) for the same tumor ROIs were estimated with the deconvolution-based CT perfusion software, in comparison with the maximum slope analysis.

- SPV is a promising semi-quantitative measurement tool of tumor perfusion, which in our series proved to correlate most strongly with the maximum slope assessed tumor blood volume.
References


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