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TECHNICAL NOTE

# CT Perfusion of the Neck: Internal Carotid Artery versus External Carotid Artery as the Reference Artery

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**SUMMARY:** Arterial selection for reference time-enhancement curve generation in deconvolution-based perfusion CT (PCT) studies of the head and neck is underevaluated. This study of 11 patients with confirmed head and neck squamous cell carcinoma demonstrates significant correlation (range, $r = 0.85–0.95$) between perfusion parameter values derived with internal carotid artery (ICA) as compared to an external carotid artery reference, supporting the use of the ICA as arterial reference in PCT studies of the neck.

Perfusion CT (PCT) is a rapid noninvasive imaging technique conceived originally to assess qualitatively and quantitatively regional cerebral blood flow (rCBF), cerebral blood volume (CBV), mean transit time (MTT), and later capillary permeability surface-area product (PS) within regions of interest (ROIs) in the brain.[1-4] Since its inception, the PCT technique has been adopted for many physiologic imaging applications, including diagnosis and management of head and neck squamous cell carcinomas (HNSCCA). In cerebral PCT, rCBF (mL/100 g/min) differs from large-vessel blood flow (mL/min) because it describes the fractional blood flow (BF) through a mass of tissue (as conducted by microvasculature) rather than flow per unit vascular volume. As such, rCBF, CBV, and MTT are useful measures for describing the perfusion of a parenchymal region of interest. The parameters generated in PCT of the head and neck are defined as fractional tissue BF (mL/100 g/min), blood volume (BV, mL/100 g), MTT (seconds), and PS (mL/100 g/min). PS, a measure of capillary permeability, was originally used as a marker for blood-brain barrier (BBB) breakdown in ischemic stroke, but PS has also been shown to correspond to the microvascular hyperpermeability seen with neoangiogenesis in brain tumors and extra-axial tumors without a BBB such as HNSCCA.[5-7] The role of PCT in the diagnosis and management of HNSCCA is continuing to expand and evolve.[6-9]

The deconvolution-based PCT technique is predicated on the central volume principle (BF = BV / MTT) and was first described in 1983 by Axel in the context of cerebral perfusion.[1] An iodinated contrast bolus is monitored as it traverses selected arterial reference, target tissue, and venous ROIs, generating time-enhancement curves proportional to contrast agent concentration. MTT can then be calculated from the arterial and tissue enhancement curves by the mathematic process of deconvolution. Dividing the area under the curve of the tissue pixel by that of the arterial pixel yields BV. The central volume equation is then solved for BF.[1-3,10]

In developmental work on PCT of the brain by Axel,[1] Lee, and colleagues, the ideal reference artery was postulated to be a vessel that was nonsupplying, large in caliber, and oriented perpendicular to the viewing plane, minimizing partial volume averaging within the selected ROI.[1-4] The internal carotid artery (ICA) and other in-plane arteries have since been used to generate adequate reference curves for acute stroke evaluation.[3,11] Current practices in PCT of the head and neck generally use the ICA, but there is little evidence supporting this practice.[6,8] The intent of this experiment was to confirm that perfusion parameter values do not significantly differ when the ICA as compared to the external carotid artery (ECA) is used a reference in HNSCCA PCT studies.

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## Technique

Fourteen patients with subsequently confirmed HNSCCA who had undergone contrast-enhanced CT and PCT as part of their routine pretreatment clinical evaluation between April and July 2002 were retrospectively evaluated. Our institutional review board approved this investigation. CT scans were obtained on a multidetector scanner (LightSpeed Ultra; GE Healthcare, Milwaukee, Wis). A localizing noncontrast CT was performed through the known primary site, and then 4 adjacent 5-mm sections at the level of the largest cross-sectional area of the tumor were selected as the area of interest for perfusion measurements. Fifty milliliters of nonionic contrast (iopamidol, Isovue, 300 mg I/mL; Bracco Diagnostics, Princeton, NJ) was injected at 4 mL/s. At 5 seconds into the injection, a cine (continuous) acquisition was initiated (120 kV, 60 mA, 4 × 5-mm sections, 1-second rotation for a duration of 50 seconds). The 1-second images were reformatted at 0.5-second intervals, and the 5-mm sections were reformatted into 10-mm sections.

Perfusion data were postprocessed by using the deconvolution technique with commercially available Perfusion 2 software on an Advantage Windows Workstation (GE Healthcare). A single observer, aware of the primary tumor site, placed a ROI on the ipsilateral ICA, internal jugular vein (IJV), and primary tumor (25–30 $mm^2$), generating contrast enhancement curves (Fig 1). Data were then processed into maps to represent PS, BV, BF, and MTT. Similarly, the same observer then reprocessed the data into maps by placing a ROI on the largest visible branch of the ipsilateral ECA, IJV, and primary tumor (25–30 $mm^2$) (Fig 2).

Quantitative measurements of BV, BF, PS, and MTT derived from ICA reference curves were individually compared with similar measurements derived with an ECA reference. Statistical analysis consisted of linear regression and Pearson product moment correlation coefficients. $P < .05$ was considered significant.

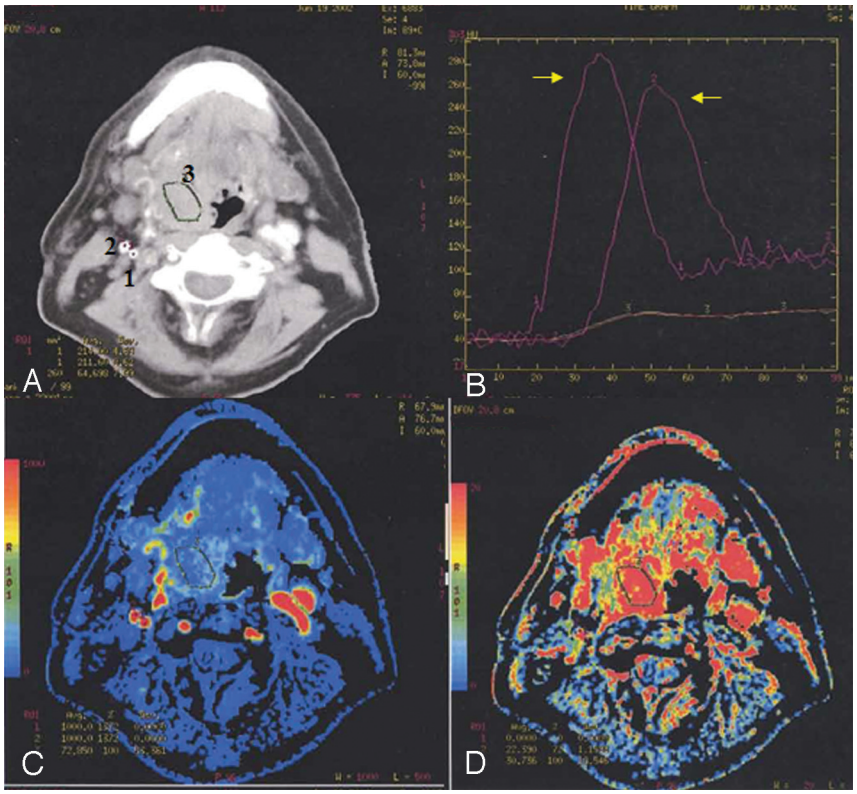


**Fig 1.** PCT imaging with ICA reference of a patient with right tongue base squamous cell carcinoma. *A*, Axial contrast-enhanced CT scan shows a mass involving the right tongue base. Regions of interest have been placed in the ICA (1), the internal jugular vein (2), and the tumor (3). *B*, Time-enhancement curve for the patient shown in *A*. The first peak is arterial enhancement; the second is venous (*arrows*). The flat curve at the bottom represents tissue region-of-interest (3) enhancement. *C*, Fractional tissue BF map for the patient in *A*. There is increased fractional tissue BF in the region of the mass lesion compared with surrounding tissue. *D*, PS map for the same patient. The tumor site displays increased capillary permeability compared with surrounding tissue.

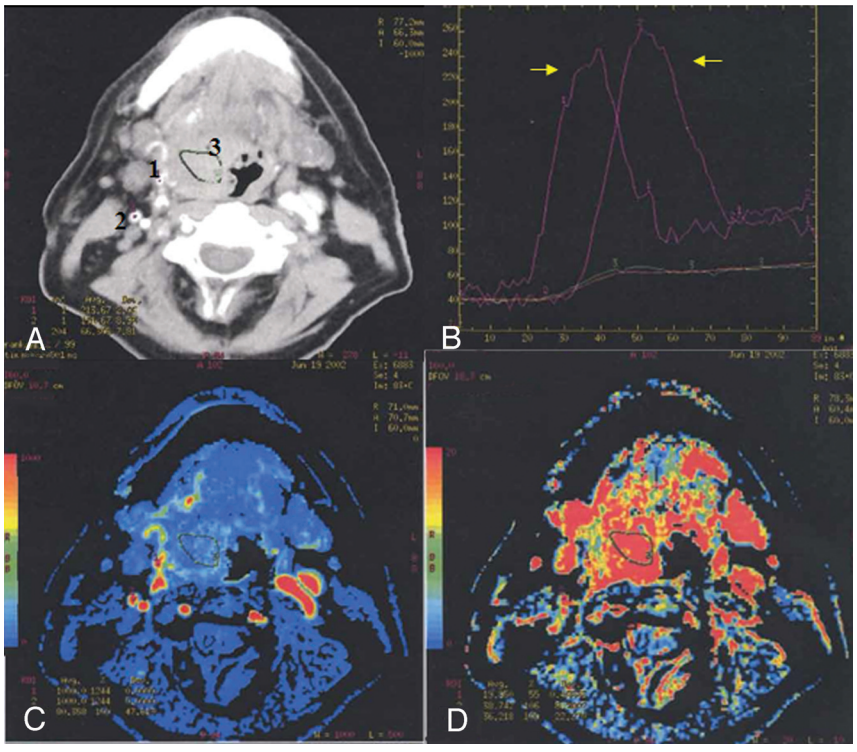


**Fig 2.** PCT imaging with ECA reference of the same patient depicted in Fig 1. *A*, Regions of interest have been placed in the ECA (1), the internal jugular vein (2), and tumor (3). *B*, Time-enhancement curve for the patient shown in *A*. The first peak is ECA enhancement; the second is venous enhancement (*arrows*). *C*, The fractional tissue BF map for the patient in *A* generated with ECA reference is similar to that generated by using the ICA as the reference function. *D*, PS map generated with ECA reference demonstrates increased capillary permeability similar to that generated by using the ICA as reference.

**Table 1: Summary of patient characteristics**

| Patient No. | Age (yr) | Sex | Tumor Location | Stage |
|---|---|---|---|---|
| 1 | 59 | M | Left tongue base | T4N2cM0 |
| 3 | 50 | F | Oral tongue | T3N0M0 |
| 4 | 49 | F | Epiglottis | T2N0M0 |
| 5 | 40 | M | Right floor of mouth | T4N2bM1 |
| 8 | 66 | M | Epiglottis | T3N0M0 |
| 9 | 41 | M | Left buccal area | T3N0M0 |
| 10 | 56 | M | Vallecula | T2N2aM0 |
| 11 | 56 | M | Right tonsil | T4N2bM0 |
| 12 | 59 | M | Right tonsil | T4N2bM0 |
| 13 | 72 | F | Left tongue base | T4N0M0 |
| 14 | 46 | M | Left tonsil | T1N2aM0 |

**Table 2: Perfusion parameter values derived with ICA and ECA reference***

| Values | ICA | ECA | Difference between Means | *P* Value |
|---|---|---|---|---|
| BF (mL/100 g/min) | 89.25 ± 34.42 | 90.93 ± 43.94 | −1.67 ± 15.17 | .7221 |
| BV (mL/100 g) | 4.07 ± 1.46 | 4.38 ± 1.78 | −0.31 ± 0.46 | .0488 |
| MTT (s) | 4.03 ± 1.36 | 4.26 ± 1.19 | −0.23 ± 0.72 | .3190 |
| Capillary PS (mL/100 g/min) | 27.68 ± 6.25 | 26.74 ± 5.45 | 0.94 ± 4.12 | .4676 |

**Note:**—ICA indicates internal carotid artery; ECA, external carotid artery; BF, blood flow; BV, blood volume; MTT, mean transit time; PS, permeability surface-area product.
* Data are mean ± SD.

## Results

Three of the original 14 patients were excluded on the basis of an inability to reliably identify the ECA. The included study group is depicted in Table 1 and comprised 8 men and 3 women with ages ranging from 40 to 72 years with a mean age of 54.0 years. Primary tumor sites included tonsil (3), tongue (3), buccal area (1), epiglottis (2), vallecula (1), and floor of mouth (1). Tumors were staged according to the tumor-node-metastasis system and were predominantly stage III (3) and IV (7) lesions but also included a stage II (1) lesion.

Values for each of BV, BF, MTT, and PS generated using the ipsilateral ICA and ECA for the reference artery were all significantly correlated (Fig 3). Pearson correlation coefficients of $r = 0.95$ for BF ($P < .0001$), $r = 0.98$ for BV ($P < .0001$), $r = 0.85$ ($P = .0009$) for MTT, and $r = 0.76$ ($P = .0065$) for PS were obtained. All correlations were significant with $P < .05$. The mean differences between values derived from ICA compared with ECA reference are included in Table 2.

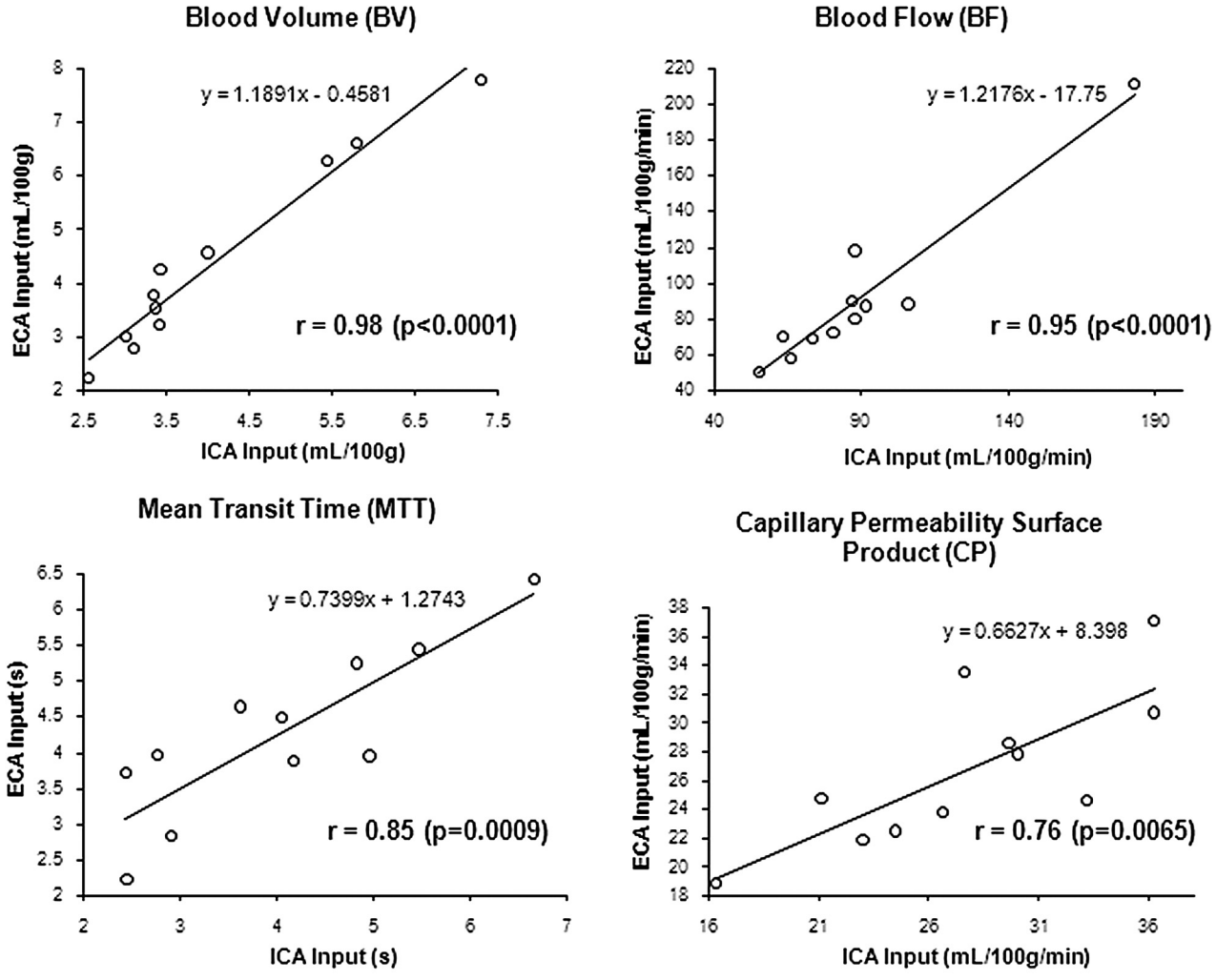


**Fig 3.** Scatterplots of perfusion parameter measurements derived with an ECA arterial reference compared with the ICA. *r* values are the Pearson product moment correlation coefficients. All correlations are significant ($P < .05$).

## Discussion

Our study specifically focused on a pretreatment population of patients with HNSCCA. The results demonstrated that BV, BF, and MTT derived from ICA reference curves were well correlated with the same measurements from ECA references, with $r$ values ranging from 0.85 to 0.98. Measurements for PS in our study were the least correlated with $r = 0.76$.

Significant correlations between ICA- and ECA-derived parameter values were supported by insignificant differences in the means for all ICA- versus ECA-derived perfusion parameters with the exception of BV (Table 2). The marginally significant difference with $P = .0488$ between BV mean values could be the result of an insufficient sample size because there is indeed a statistically significant strong correlation ($r = 0.98$) between ICA- and ECA-derived BV values as described above.

In a previous PCT study of benign and malignant head and neck lesions, 4 of which were subsequently determined to be HNSCCA, Rumboldt et al[9] found no significant perfusion parameter variance with the use of the ICA compared with ECA reference. The confirmatory evidence presented here supporting the use of ICA reference in HNSCCA PCT studies is important to document as this technique gains greater acceptance for assessing treatment response and differentiating recurrent tumor from posttreatment changes.

Limitations to this study include the relatively small sample size and the exclusion of those patients whose ECAs were not reliably identified in cross-section, conceivably a source of selection bias. If, for example, ill-defined ECA branches were associated with hemodynamically compromised neck vasculature (ie, extensive atherosclerosis with stenoses differentially affecting the ICA compared with the ECA), the correlation between ECA- and ICA-derived parameters could have been overestimated. Also, our study identified the ECA and its branches on noncontrast images. Arterial identification on contrast-enhanced images would be an improvement in future studies.

## Conclusions

This study demonstrated a significant correlation between the PCT measurements of BV, BF, and MTT derived with ICA reference as compared with ECA reference. These results support the use of the ICA as a reference artery in PCT imaging of HNSCCA, though further studies with larger patient populations are needed to confirm these findings.

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