Multidetector Computed Tomography Perfusion in Head and Neck Squamous Cell Carcinomas: Evaluation of a Dose Reduction Strategy

Shuchi Bhatt[1] Samrat Mandal[1] Gopesh Mehrotra[1] Vipin Arora[2] Usharani Singh[3]

[1] Department of Radio-diagnosis, University College of Medical Sciences, University of Delhi, Delhi, India
[2] Department of Otorhinolaryngology, University College of Medical Sciences, University of Delhi, Delhi, India
[3] Department of Pathology, University College of Medical Sciences, University of Delhi, Delhi, India

Address for correspondence Shuchi Bhatt, MD, FICRI, MNAMS, A-249, Surya Nagar, Ghaziabad 201011, Uttar Pradesh, India (e-mail: shuchibd71@gmail.com).

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Abstract

Background Computed tomography perfusion (CTp), a useful technique in oncology, is not widely utilized due to the high radiation dose delivered from it. It involves scanning the region of interest every second for 50 seconds following intravenous contrast administration. Doubling sampling interval (SI) to 2 seconds will half the radiation dose, but may impact its effectiveness, which needs to be evaluated.

Objectives To evaluate a dose reduction strategy in CTp by determining agreement between standard dose (SD) CTp (acquisition with SI 1 second) and low-dose CTp techniques with SI of 2 seconds (achieved either by reconstruction only or true low-dose acquisition).

Materials and methods This cross-sectional study was conducted on histopathology-proven head and neck squamous cell carcinoma (HNSCC) patients who underwent CTp on 64 slice multidetector CT. A total of 56 patients had SD and 24 patients underwent true low dose (LD) acquisition. SD data were also reconstructed at SI 2 seconds to obtain a dataset simulating low dose (low-dose reconstruction [LDr]). Paired *t*-test was applied to compare CTp in SD and LDr groups and the Bland–Altman plot drawn to calculate 95% confidence limit of agreement. The Kolmogorov–Smirnov test compared CTp parameters for LDr and LD groups.

Results There was no statistical difference in CTp parameters (except blood flow in malignant) in SD and LDr groups for both malignant and normal tissues. CTp of malignant tissue was not statistically different in LDr and LD groups but the radiation dose was half in the LD group.

Conclusion Reduction of radiation dose to half achieved by doubling the SI does not affect the CTp parameters significantly. So LD acquisitions will increase the use of CTp in HNSCC.

Keywords
- CT perfusion
- sampling interval
- dose reduction
- head and neck
- squamous cell carcinoma

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Introduction

Head and neck cancer is the eighth most common cause of cancer death worldwide[1] and accounts for 25% of male and 10% of female cancers in India.[2] Squamous cell cancer (SCC) is the predominant histology present in 90% of head and neck cancers.[3] Diagnosis is based on clinical examination and confirmed by histopathological examination. To assess the loco-regional extent of the tumor and the lymph-node involvement, computed tomography (CT)/magnetic resonance (MR) imaging is required. Advances in oncology with the use of neo-adjuvant and anti-angiogenic therapy also demand evaluation of tumor behavior through functional imaging like positron emission tomography imaging,[4] diffusion MR or MR spectroscopy,[5] or perfusion studies.[6] Noninvasive evaluation of hemodynamics/microcirculation of the neoplasms can be done by determining the contrast kinetics as the contrast passes through the tumor and can be quantitatively estimated by CT perfusion (CTp) parameters—blood flow (BF), blood volume (BV), permeability surface (PS), and mean transit time (MTT). CTp in head and neck squamous cell carcinoma (HNSCC) has wide applications and has been utilized to assess treatment response, detect lymph-node metastases, recognize recurrence, and accurately differentiate tumor from normal tissue.[7–9] Combining CTp with routine contrast-enhanced CT (CECT) study would provide both the functional and morphological assessment, respectively, in the same setting.

Technically CTp is a dynamic CECT examination done for a selected slice thickness which is continuously irradiated over a time frame close to a minute, delivering a high radiation dose to the patient, thus, reserving its use. The estimated dose in CTp, therefore, is dependent upon the exposure factors—kilovoltage (kV), the milliampere (mA), the beam thickness, the selected slice thickness (slice thickness depends upon the type of MDCT scanner used), the radiosensitivity of the irradiated organs, and the total time of scanning. In a standard CTp exam of head and neck, acquisition is done every second for 50 seconds obtaining data from 50 time points. The time interval between the two scans is defined as the sampling interval (SI), which is 1 second in a standard CTp acquisition. A reduced dose protocol (reduced tube potential and/or tube current) can achieve dose reduction only to a certain extent as a simultaneous increase in image noise decreases the image quality. Another theoretical concept for dose reduction would be to increase the SI to 2 seconds (scanning every 2 seconds instead of 1 second) for the same scan duration; reducing the radiation exposure to half of the actual CTp dose. As this involves acquisition at alternate time points, the data would also be halved which might impact the results of the CTp study. As the effect of increasing SI on CTp measurements is still unclear, we made an attempt to evaluate the dose reduction strategy of doubling the SI from 1 second to 2 seconds in HNSCC. The CTp datasets with doubled SI of 2 seconds can be achieved by acquiring the scan with SI of 2 seconds. However, a similar dataset was created by reconstructing the standard CTp (acquired with SI 1 second) by using data from alternate time points (that is every 2 seconds). This dataset obtained by the reconstructive technique simulates a low-dose acquisition with data acquired every 2 seconds, simulating a SI of 2 seconds. *Therefore, the resultant data are actually halved compared with the standard acquisition every 1 second.*

Based on the SI used for acquisition and reconstruction of CTp scan, three groups were formed as depicted in ►**Table 1**.

Aims

To evaluate a dose reduction strategy by doubling the sample interval from 1 second to 2 seconds for CTp in HNSCC. Objectives were to determine the agreement between standard dose (SD) CTp and reconstructed low dose (LDr) CTp and to compare LDr CTp with true low dose (LD) CTp. The secondary objective was to calculate interobserver variation of CTp parameters in different groups (SD, LDr, and LD).

Groups were obtained as follows:

- SD CTp: standard acquisition (SI 1 second) and standard reconstruction (SI of 1 second).
- LDr CTp: standard acquisition (SI 1 second) with LDr (SI 2 seconds).
- LD CTp: low-dose acquisition (SI 2 seconds) with LDr (SI 2 seconds).

Table 1 The three datasets—"standard dose," "low-dose reconstruction," and "low dose"—used for the study

CTp acquisition	Sampling interval for acquisition (SI)	Sampling interval for reconstruction (SIR)	Group according to SI of CTp scan	CTp technique with respect to radiation dose	
Standard ($N = 56$ patients)	1 s	1 s	Standard dose (SD)	Standard dose	Standard dose
		2 s[a]	Low-dose reconstruction (LDr)[b]	Simulation	Low dose
Doubled SI (24 patients)	2 s[c]	2 s	Low dose (LD)	True low dose	

Abbreviation: CTp, computed tomography perfusion.
[a]Doubling the SI to 2 seconds during reconstruction of the standard SI 1 second acquisition resulted in a low-dose reconstruction which was only a simulation of the low dose CTp technique.
[b]This is actually a low-dose simulation as only reconstruction is done at SI 2 seconds after acquisition at 1 second.
[c]However, acquiring the data with 2 seconds SI resulted in the true low-dose CTp scan.

Materials and Methods

Patient Selection

After due approval of Institutional Ethics Committee-Human Research, a cross-sectional study was conducted in a tertiary care hospital over a period of 16 months. Adult patients of either gender with a clinically apparent neck mass or lesion detected on imaging/indirect laryngoscopy and proved to be SCC on histopathology and had not received any treatment were included in the study after taking a written informed consent. HNSCC of peripheral nervous system and nasopharyngeal region, partially treated, recurrent disease, patients allergic to contrast, or having deranged renal function tests, poor general condition, underwent recent biopsy (<2 weeks), and pregnant patients were excluded. All selected patients underwent CTp of the neck mass.

Sample Size

In a previous study[1] the estimated BF for CTp at SI of 1 second and 2 seconds was 118.8 ± 47.8 and 127.7 ± 56.7 mL/min/100 g, respectively, with the mean change being 8.9 mL/min/100 g and the standard deviation of change being 26.60. For the study to have 80% power and 5% level of significance under paired design, a sample size of 56 was required for comparing CTp data obtained with two different techniques. So our sample size for standard acquisition dataset was set to 56. As no comparable study was available for low-dose acquisition with SI of 2 seconds, an arbitrary number of 25 patients were chosen but one patient had a technically inadequate scan.

Methodology

The history, general and local physical examination, previous imaging studies, and histopathological findings were recorded. All patients underwent CT neck examination, on a 64-slice MDCT scanner (Somatom Definition; Siemens AG Healthcare Sector, Erlangen, Germany).

Technique of CT Examination

After overnight fasting, a CECT and CTp scan were acquired in the same setting. 18 G intravenous cannula was placed in the antecubital vein opposite the side of lesion for CTp study. The sequence of examination was noncontrast CT (NCCT), dynamic CT, and CECT scan. The pre- and postcontrast scans were done with acquisition parameters of 120 kVp, 110 mAs, rotation time 1 second, table feed 48 mm/rotation, slice thickness 5 mm with 64×0.6 collimation, and a field of view (FOV) of 200 mm.

CTp was planned for the lesion on the NCCT scan and acquired with a delay of 6 seconds after administration of 50 mL of nonionic iodinated contrast agent (350 mg/dL), injected at a rate of 5 mL/s using a dual-head power injector followed by 20 mL saline bolus at the same rate. The acquisition parameters used were 80 kVp, 100 mAs, rotation time of 1 second, 0 table feed, slice thickness 2.5 mm,64×0.6 collimation, and a FOV of 200. Gentle breathing was allowed but the patient was instructed not to swallow during the scan. In the SD group, SI was 1 image/second and for LD group it was 1 image/2 seconds.

The NCCT and postcontrast scans were acquired from the skull base to the thoracic inlet after a further intravenous administration of 60 mL of contrast at 4 mL/s and a delay of 35 seconds. The final study group had 80 patients: 56 patients had standard acquisition (SI = 1 second) while 24 patients had low dose acquisition (SI = 2 seconds). Standard acquisition was also reconstructed considering data from alternate time points (with reconstruction SI of 2 seconds) to obtain LDr data simulating a low-dose acquisition.

Therefore, three datasets obtained were: SD ($n = 56$); LDr ($n = 56$); LD ($n = 24$).

Data Postprocessing and Image Analysis

The CTp data were transferred to the workstation to calculate the CTp parameters using Siemens Volume perfusion CT body software based on a deconvolution method. The region of interest (ROI) was placed within the external/internal carotid artery. Time attenuation curves were obtained after motion correction (►**Figs. 1** and **2**). Parametric maps for BF, BV, MTT, and PS were generated (►**Fig. 3**). The level with the largest cross-sectional area of tumor was chosen and a user-defined ROI was drawn freehand, incorporating the solid, homogeneously perfused tumor portions while omitting any necrotic regions. Care was taken not to include any surrounding vessel. CTp parameters were calculated for the tumor and also for normal structures (muscle, small lymph nodes <1 cm size, salivary glands, and thyroid gland).

The following CTp parameters were calculated: MTT in seconds; BV in mL/100 g; BF in mL/100 g/min; PS area product in mL/100 g/min.

Two blinded reviewers independently calculated the CTp parameters for the three groups.

The scanning length, CT dose index volume (CTDIvol), and dose-length product (DLP) for the CECT (NCCT and post contrast) and perfusion scans were recorded and radiation dose calculated using the Monte Carlo method of dose estimation.

Statistical analysis was performed using software Graphpad Prism 7 (Graph Stats Technologies Private Limited, Bangalore, Karnataka, India) for windows version 7. Intraclass correlation was calculated using software Medcalc version 17.4.4. All CTp values were presented as mean ± standard deviation. Statistical analyses of the obtained perfusion values in SD and LDr groups were done using the parametric test for both normal and malignant structures separately. Bland–Altman plots were drawn and 95% confidence limits of agreement were calculated; limit of agreement being mean difference ± 2 SD. A nonparametric Kolmogorov–Smirnov test was used to compare CTp parameters for the LDr and LD groups. Intraclass correlation was calculated to determine the interobserver agreement for the entire dataset for both the malignant and normal tissues.

Results

The final study group constituted 80 patients, 56 patients with standard CTp study (SI 1 second) and 24 patients with doubled sample interval (SI 2 seconds) CTp study. Three sets

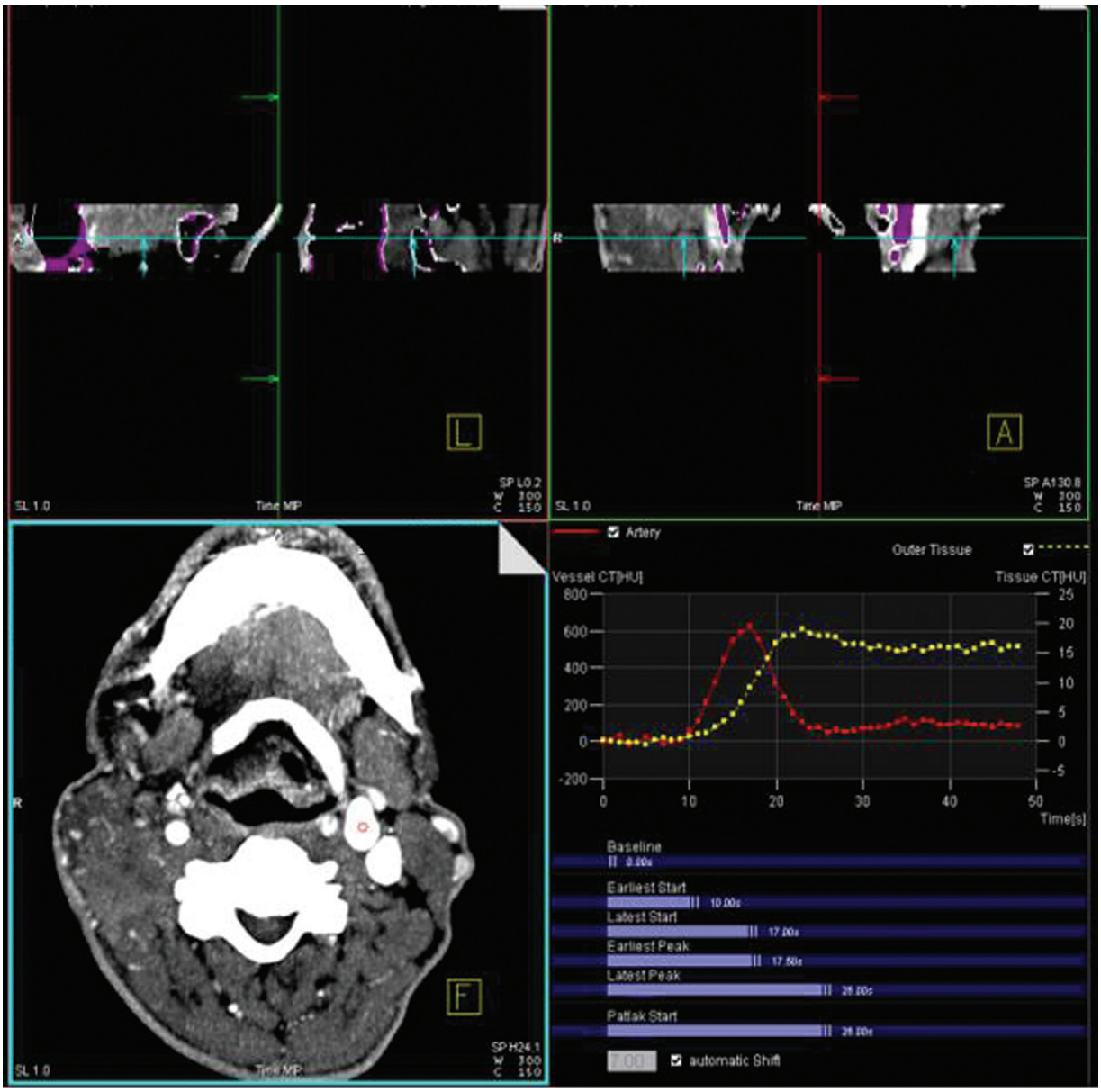

Fig. 1 Placement of ROI in carotid artery and generation of time attenuation curve. The sample interval was 1 second and CT perfusion acquisition was done for 50 seconds. So the time attenuation curve has 50 sample points (SD). CT, computed tomography; ROI, region of interest; SD, standard dose.

of CTp parameters were obtained in each patient namely SD, low-dose simulation (LDr), and LD. CTp parameters calculated were BV, BF, PS, and MTT. For malignancy the CTp parameters were determined for all SD, LDr, and LD groups, while for the normal tissues CTp parameters were determined only for SD and LD groups as depicted in ►**Table 2**.

Agreement of Perfusion Parameters (CTp) between SD and LDr for Normal and Malignant Tissues

The perfusion parameters were logarithmically transformed to make them follow normal distribution and agreement was tested between various values of BV, BF, PS, and MTT between the two groups using paired *t*-tests. Bland–Altman analysis was further done to test the agreement between the two groups for individual cases for CTp parameters—BF, PS, and MTT for malignant tissue (►**Table 3**) and normal tissue (►**Table 4**).

BF values in the SD and LDr groups were significantly (p-value = 0.003) different in the malignant tissues.

Matched paired *t*-tests between the two groups SD and LDr for normal tissue and malignant tissue show that there was no significant statistical difference between the two means for rest of perfusion parameters. In most cases, it was observed that for all CTp parameters, the individual observations were between the 95% limits of agreement. The overall bias tended toward the mean difference of zero.

Comparison of CT Perfusion Parameters between True and Reconstructed Low-Dose CTp Scan for Malignant Tissue

The CTp parameters as well as their logarithmic transformations were tested for normality using the D'Agostino–Pearson

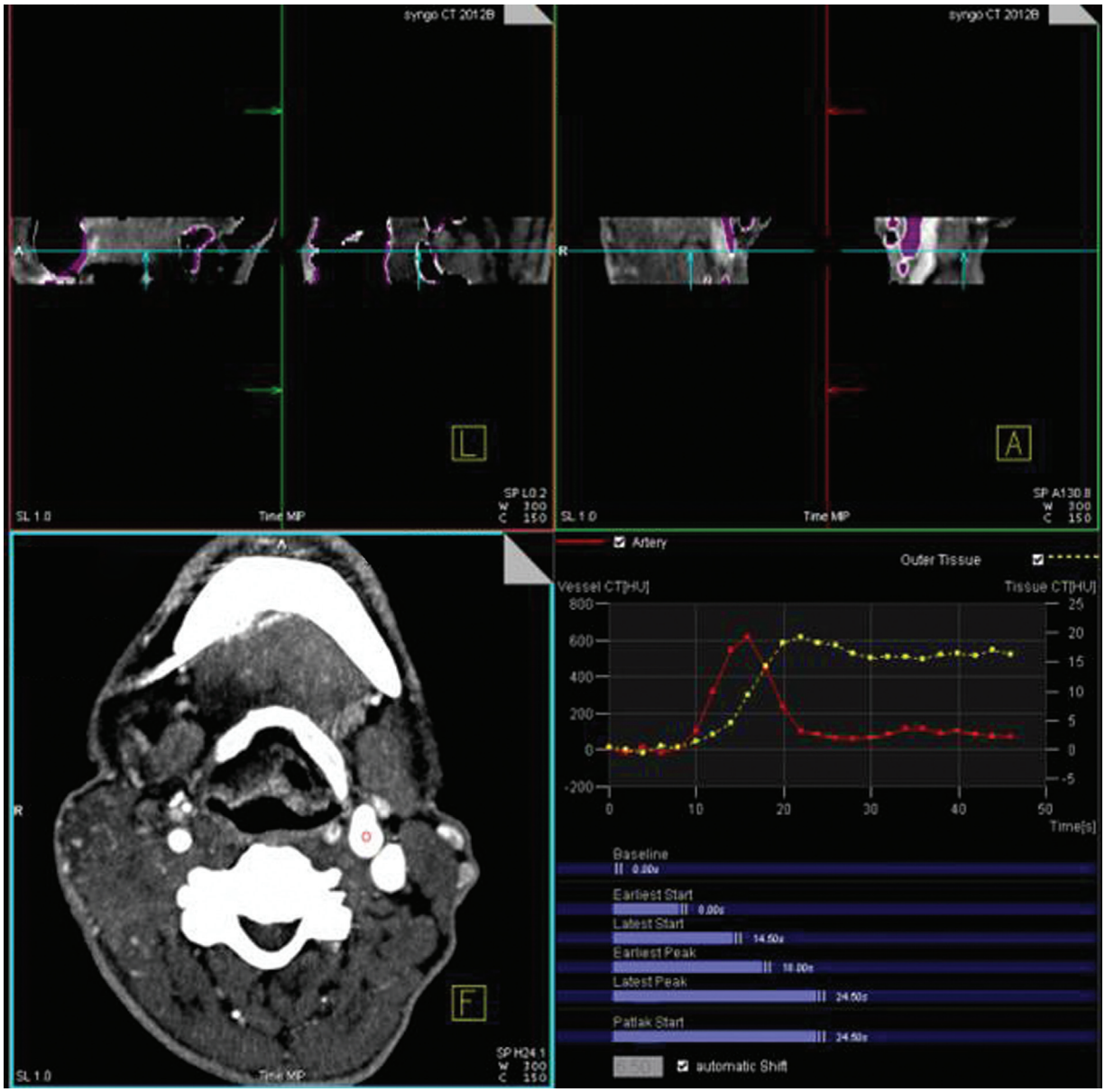

Fig. 2 Generation of time attenuation curve for the same patient shown in ►**Fig. 1** with sample interval of 2 seconds. The time attenuation curve spans for 50 seconds but there are 25 sample points (LDr). LDr, low-dose reconstruction.

omnibus test for LD and LDr and as they were not normal, the nonparametric Kolmogorov–Smirnov test was used to compare CTp parameters (►**Table 5**). There was no statistically significant difference between the CTp parameters BV, BF, PS, and MTT, analyzed by the Kolmogorov–Smirnov test between the two groups.

Intraclass Correlation for Different CTp Parameters among Two Observers for Both Normal and Malignant Tissues

The intraclass correlation coefficients (ICCs) were very high for BF (normal: 0.9 and malignant: 0.88), high for BV (normal: 0.82 and malignant: 0.79), PS (normal: 0.77 and malignant: 0.74), and acceptable for MTT (normal: 0.6 and malignant: 0.57) (►**Table 6**).

Radiation Dose

The effective dose received by the patient during the dynamic scan of CTp study obtained with the standard protocol of SI of 1 second was estimated to be to be 4.73 mSv. However, the low-dose scan acquired at a SI of 2 seconds was exactly half of the standard protocol. One NCCT/postcontrast scan obtained delivered 1.38 ± 0.18 mSv to the patients.

Discussion

Several studies have determined BF, BV, PS, and MTT values in malignant SCCs of head and neck region: Tawfik et al,[10] Faggioni et al,[3] Trojanowska et al,[11] and Jo et al.[12] The main reason for variability in CTp parameters in these studies is due to use of different postprocessing software

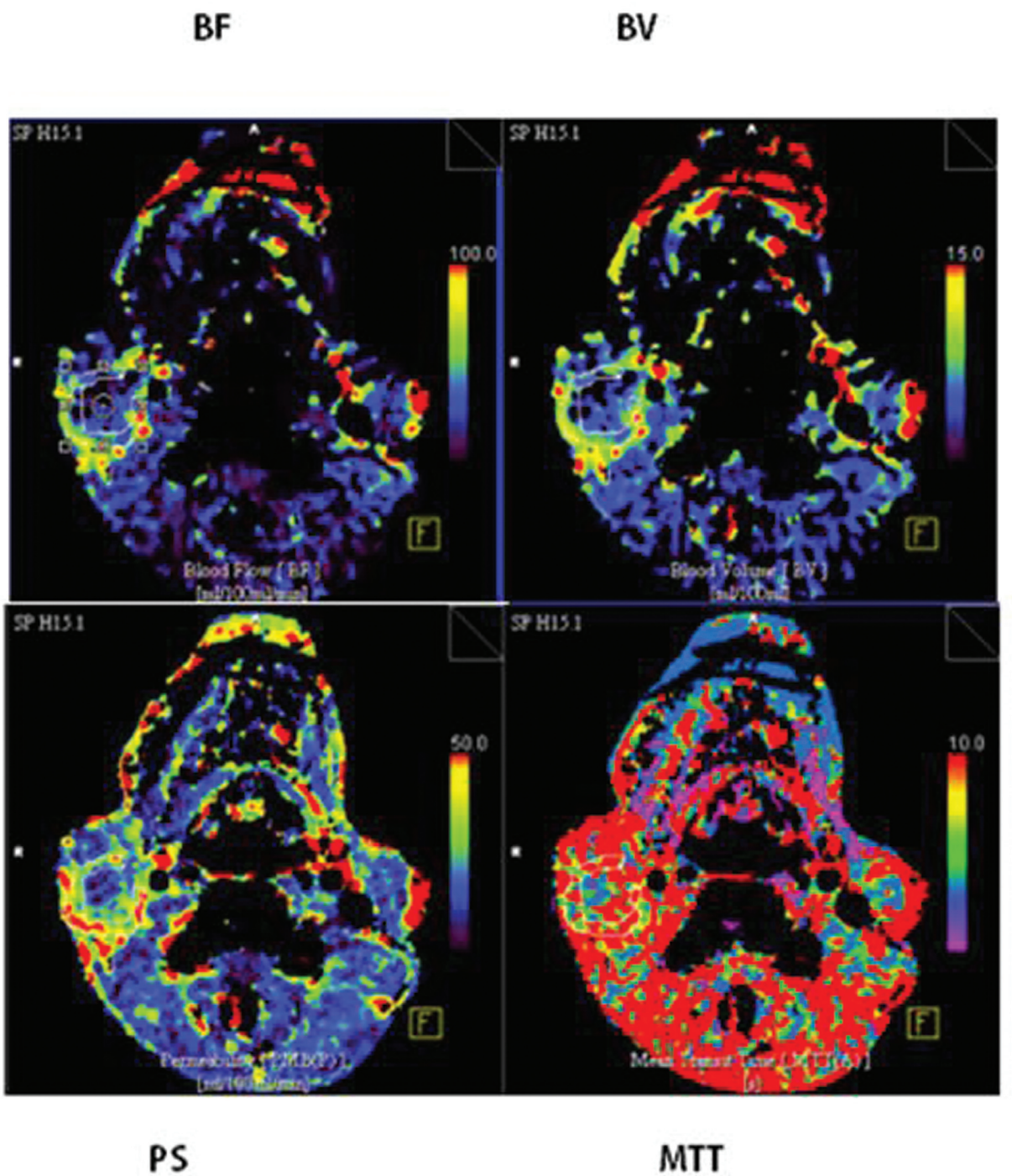

Fig. 3 Generation of parametric maps for BF, BV, PS, and MTT. BF, blood flow; BV, blood volume; MTT, mean transient time; PS, surface permeability.

provided by different vendors.[13] It is also believed that acquisition factors—tube potential, tube current, total scan time, and scan interval—all play a role in determination of perfusion parameters. Variation can also occur due to ROI placement such as inclusion/exclusion of vessels piercing through the malignant tissue. Observer interaction with software programs can be a source of variability. Given the great variability, CTp values in our study of all three sets (SD, LDr, and LD) are within an acceptable range. In our study, two reviewers independently determined the CTp parameters for both the malignant and normal tissues. The ICCs were very high for BF (0.9 and 0.88), high for BV (0.82 and 0.79) and PS (0.77 and 0.74), and acceptable for MTT (0.6 and 0.57) for normal and malignant tissues, respectively. Our results are in concordance with those of Petralia et al,[8] who calculated the ICCs for three reviewers to be 0.98, 0.98, and 0.98 for BF; 0.88, 0.91, and 0,95 for BV; 0.78, 0.77, and 0.94 for MTT, and 0.67, 0.94 and 0.65 for PS. The maximum correlation was noted for BF and BV parameters in both studies.

Table 2 Range, mean, and standard deviation of CT perfusion parameters in groups SD, LDr, and LD for malignant tissue and SD and LD for normal tissues

	Group	Blood volume (BV), mL/100 g		Blood flow (BF), mL/100 g/min		Mean transient time (MTT), s	Surface permeability (PS), mL/100 g/min		
		Range	Mean ± SD (standard deviation)	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
Malignant tissue	SD	0.1–23	11.2 ± 4.3	0.4–189	59..8 ± 27.3	3.0–17	8.7 ± 3.5	4.6–60	27.3 ± 11.1
	LDr	0.8–30	11.1 ± 4.7	2–149	53.7 ± 25.5	03.0.-18	8.4 ± 3.4	3.1–72	27.0 ± 11.6
	LD	6.4–18	11.4 ± 3.6	29.2–70	51.3 ± 13.3	3.9–20	9 ± 4	16.5–42.8	28 ± 9.8
Normal tissues									
Tongue	SD	0.2–7	2.9 ± 1.6	0.6–28.5	10.7 ± 5.8	3.4–40	13.4 ± 7.8	1.2–26.8	12.2 ± 5.4
	LD	0.1–7	2.9 ± 1.6	0.4–26.7	10.3 ± 6.0	4.4–39.7	12.5 ± 7.5	0.3–20.9	11.1 ± 4.3
LN	SD	0.6–11	6.7 ± 3.1	3.3–63	30.9 ± 15.8	7.6–42	33.9 ± 10.4	3–22.4	10.7 ± 5.6
	LD	0.7–13	7.3 ± 3.6	2.6–70	31.7 ± 18.5	4.7–40	22.4 ± 11	3–20.6	11 ± 5.3
Muscle	SD	0.1–8.5	2.4 ± 2.2	0.4–49	10.4 ± 11.0	2.7–34	10.2 ± 6	2.3–24.2	11.7 ± 5.4
	LD	0.2–9.1	2.6 ± 2.3	1.0–39	9.3 ± 9.8	2.7–36	10.1 ± 6.5	2.7–25	11.8 ± 5.0
Salivary gland	SD	5.0–18	12 ± 4.5	20–95	59.9 ± 25.9	5.1–399.1	68.9 ± 105.3	3.5–27.7	14.3 ± 5.5
	LD	3.2–18	11.8 ± 5	15.2–90	55.2 ± 26.1	16.9–70.8	40.5 ± 14.2	5.8–21	14.0 ± 3.7

Abbreviations: CT, computed tomography; LD, low dose; LDr, low-dose reconstruction; SD, standard dose.

Table 3 Agreement of CT perfusion parameters between groups SD and LDr for malignant tissue and Bland–Altman analysis to test the agreement between the two groups SD and LDr for individual cases for the CT perfusion parameters

	Agreement using paired *t*-test			Bland–Altman analysis (for individual cases)		
Perfusion parameters	Difference (mean ± standard deviation)	Confidence interval	*p*-Value	Bias	Standard deviation of bias	95% Limits of agreement
BF	0.04 ± 0.1	0.01–0.07	**0.003**	NA	NA	NA
BV	−0.005 ± 0.12	−0.06	0.72	−0.01	**1.9**	**−3.7 to 3.9**
MTT	0.013 ± 0.16	−0.08	0.53	−0.25	2.6	−4.8 to 5.6
PS	0.01 ± 0.12	−0.06	0.48	−0.35	7.3	−13.9 to 14.6

Abbreviations: BF, blood flow; BV, blood volume; CT, computed tomography; LD, low dose; LDr, low-dose reconstruction; MTT, mean transient time; PS, surface permeability; SD, standard dose.
Note: NA, not available, not determined as BF was significantly different in the two datasets as shown by values in bold.

Correlation of CTp Parameters between SD and LDr (Low-Dose Simulation) Datasets

Various studies have attempted to reduce the radiation by reducing tube voltage and tube current but have failed beyond a certain limit due to degradation of image quality. Most studies of HNSCC have used SI of 1 second, thus, scanning the predetermined ROI every second. If perfusion data are acquired every 2 seconds, it is expected to lower the radiation dose to half. During postprocessing by reconstructing the acquired (SI 1 second) data at 2 seconds SI, we achieved a dataset simulating a low-dose acquisition (SI 2 seconds) and named it LDr. Another dataset obtained by reconstruction with SI 1 second represented the SD data. We compared the mean and standard deviations of both these datasets (SD and LDr) for all four CTp parameters (BF, BV, MTT, and PS) in both malignant and normal tissues by matched paired *t*-tests. We found that except for BF in malignant tissues, all CTp parameters in the two datasets did not have statistically significant difference among them. We further confirmed our agreement between the two datasets by plotting the Bland–Altman plot for individual cases for each CTp parameter in normal and malignant tissues (except for the BF parameter in malignant tissue). All the Bland–Altman plots revealed that most cases were between the 95% confidence interval and the bias was close to zero, thus confirming our results. Our results are similar with those of Tawfik et al,[10] who had inferred that all four parameters (BV, BF, PS, and MTT) did not have any statistical difference between the two datasets obtained with SI 1 and 2 seconds in HNSCC. Our study is superior to their study due to a greater sample size (80 in our study vs. 24 in Tawfik et al) and besides comparing CTp in malignant tissues, we also evaluated normal tissues.

Table 4 Agreement of CT perfusion parameters between groups SD and LDr for normal tissue and the corresponding Bland–Altman plots are plotted and show agreement between the values for all CT perfusion parameters

	Agreement using paired *t*-test			Bland–Altman analysis		
Perfusion parameters	Difference (mean ± standard deviation)	Confidence interval	*p*-Value	Bias	Standard deviation of bias	95% Limits of agreement
BF	0.01 ± 0.18	−0.07	0.444	0.7189	5.441	−9.946 to 11.38
BV	−0.02 ± 0.21	−0.073	0.147	0.02992	1.792	−3.5 to 3.5
MTT	−0.007 ± 0.20	−0.028	0.681	−0.09606	3.954	−7.8 to 7.6
PS	0.02 ± 0.18	−0.051	0.191	3.216	32.6	−60.7 to 67.1

Abbreviations: BF, blood flow; BV, blood volume; CT, computed tomography; LD, low dose; LDr, low-dose reconstruction; MTT, mean transient time; PS, surface permeability; SD, standard dose.

Table 5 Comparison of CT perfusion parameters between groups LDr ($n = 56$) and LD ($n = 24$) for malignant tissue

CT perfusion parameter	Kolmogorov–Smirnov D-statistic	Approximate *p*-value
Blood Volume (BV)	0.1791	0.876
Blood flow (BF)	0.1906	0.8239
Surface permeability (PS)	0.194	0.807
Mean transit time (MTT)	0.2067	0.7411

Correlation of CTp Parameters between Two Low-Dose Datasets (Low Dose Simulation/Reconstructed Low Dose) and (True Low Dose) Datasets

To validate the results of dose reduction by increasing the SI to 2 seconds, we correlated two sets of low-dose CTp parameters—LDr (acquired at SI 1 second but reconstructed at 2 seconds) with LD (directly acquired at SI 2 seconds). Thus, both datasets represented half the time points compare with that in the standard acquisition with 50 time points in a 50 second dynamic acquisition with SI of 1 second. Being a reconstructive technique, the low-dose simulation (LDr) CTp hypothetically reduced the radiation dose to half, whereas LD delivered just half the radiation compared to that in a standard acquisition. As the sample size was less (24 patients), we tested difference in means and standard deviations between the two datasets by the nonparametric Kolmogorov–Smirnov test. There was no statistically significant difference between all the four CTp parameters BV, BF, PS, and MTT by the Kolmogorov–Smirnov test for malignant tissues. Till date, there has been no published study which has evaluated the CTp technique acquired at 2 second SI. Thus, this pilot study opens future avenues for low-dose CTp studies for HNSCC, which will deliver just half the radiation dose but provide the same hemodynamic information for HNSCC.

Radiation Dose of CTp

The radiation dose (CTDIvol) can be as high as a DLP of 1,905 mGy cm corresponding to an equivalent dose of 10.3 mSv with scanning parameters of 120 kV and 100 mAs.[14] However, use of low tube voltage and tube current modulation techniques lowers the radiation dose (DLP 205 to 554 mGy cm) in CTp imaging of head and neck tumors.[15] Tawfik et al[10] similarly found a DLP of 375.2 mGy cm with the use of 80 kV and 100 mAs. In our study, identical acquisition parameters resulted in an effective dose of 4.73 mSv (DLP of 801.3 mGy cm) with the use of SI of 1 second, but with double SI of 2 seconds the radiation dose was halved (2.37 mSv, DLP of 400.65 mGy cm).

Table 6 Intra-class correlation (ICC) for different CT perfusion parameters among two observers for both normal and malignant tissues ($n = 80$)

	Normal tissues			Malignant		
CTP	ICC	95% Confidence interval		ICC	95% Confidence interval	
BV	0.82	0.72	0.88	0.79	0.67	0.86
BF	0.9	0.85	0.94	0.88	0.81	0.92
MTT	0.57	0.39	0.72	0.56	0.38	0.71
PS	0.72	0.65	0.85	0.74	0.61	0.83

Abbreviations: BF, blood flow; BV, blood volume; CT, computed tomography; MTT, mean transient time; PS, surface permeability.

Conclusion

There was no statistical difference in CTp parameters (except BF) of SD, LDr (low-dose simulation), and LD CTp scans of malignant tissues. Therefore, a low-dose CTp study acquired with a double SI of 2 seconds will give similar CTp values as a standard-dose CTp study with SI of 1 second, while achieving a reduction in *radiation* dose to half. Thus, a markedly reduced *radiation* dose in a CTp should encourage more regular use of CTp techniques in HNSCC patients.

None used. This work has not been published previously or sent for any publication elsewhere. Publication is

approved by all authors and explicitly by the responsible authorities. If accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright holder. Tables 1 to 6 are based on authors' own work.

Conflict of Interest
None.

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