Differences in perfusion CT parameter values with commercial software upgrades: algorithm consistency and stability

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Purpose

Computed tomographic (CT) perfusion imaging is a widely applied technique for the evaluation of acute ischemic stroke patients and to assess other brain diseases, including tumors [1,2]. It is also a promising technique that realizes functional imaging, as an adjunct to a morphologic CT examination, that can be used as an aid to carefully evaluate the response to therapy in oncologic patients, especially with the new therapies [3,4]. This technique has increased in the past few years, thanks to the diffusion of commercial Perfusion CT software platforms that are now integrated into a clinical reporting workstation. Although one of the advantages of CT perfusion imaging is its ability to allow quantitative results, it has been reported that the CT perfusion imaging maps and relative quantitative results were significantly different among commercial software programs, provided by various CT manufacturers, using different algorithms, even when using identical source data, presumably because of differences in tracer-delay sensitivity [5] and between different versions of the same software platform [6]. V. Goh et al have demonstrated that upgrades of the same software (version 3.0 and 4.0 of perfusion software GE Healthcare Technologies) may alter the derived parameter values in colorectal cancer because of the introduction of T0, the time difference in arrival of contrast within the input vessel and the tissue of interest in version 4.0 [6]. Beyond this previous study and considering the recent introduction of the new version of upgrades of a widely-used commercial software platform (Perfusion 4.0 to 4D; GE Healthcare Technologies), the aim of our study was to determine how commercial software upgrades impact on algorithm consistency and stability among the three version upgrades of the same software platform (versions 3.0, 4.0 and 4D; Perfusion CT software, GE Healthcare Technologies).
Methods and Materials

1. Measurements.

Blood Volume (BV), Blood Flow (BF), Mean Transit Time (MTT) and Permeability Surface area product (PS) were calculated with repeated measurements (n=304) while truncating the time density curve (TDCs) at different time values in 6 CT perfusion studies conducted for lung cancer during chemotherapeutic treatment (LC1, LC2), Hodgkin Lymphoma (HL1, active, and HL2, inactive) and renal cell carcinoma (RCC1, RCC2), performed with a 64-section multi-slice CT scanner (VCT, GE Healthcare, Milwaukee, Wis.), from June 2009 to August 2011 following ethical approval. The median acquisition time of CT perfusion studies was 54.6 seconds (range 48.3-60 seconds). In Table 1, the main features of the 6 CT perfusion studies selected to realize our work are reported.

All 6 CT perfusion studies were analyzed in consensus by two radiologists (with 5 and 2 years experience interpreting perfusion CT images, respectively) by using commercially available software (Body Tumour CT Perfusion software version 4D; GE Healthcare Technologies). The arterial input was determined by placing a circular ROI, with a diameter of no more than half the arterial diameter, within the aorta, these are always shown in the field of view. A TDC for the entire acquisition time of each study was generated automatically. Perfusion parameters of the selected tissue were measured on a circular or oval ROI around the peripheral margin of the lesion with an electronic cursor and mouse. Large ROI (i.e. a ROI larger than 70% of the minimum diameter of the tumor) was chosen to incorporate the solid-appearing part of the target lesion, but care was taken to avoid atelectatic tissue, cystic, calcification and cavitation. For each patient the arterial and tissue ROI maintained fixed during all the measurements, while truncating the TDC positioning the first cursor at the last time before the start of the slope of the TDC and the second cursor at any time indicating the temporal resolution from that, to allow the processing of the data to the end of the TDC. Mean values were recorded for each parameter: BF, BV, MTT and PS. Analysis was repeated in the same manner using the previous version of the same platform (Perfusion software version 3, Perfusion 3; Perfusion software version 4, Perfusion 4; GE Healthcare Technologies). Because of the presence of three cursors for truncating the TDC, in version 3 and version 4 of CT perfusion software, the second and the third cursors were located coincidentally along the TDC at the same time as those located by the second cursor in version 4D. All ROI, both for arterial input and target lesion, defined for each study were saved within the software platform to subsequently enable an identical placement at the same lesion axial slice level for the three different versions.
2. Statistical Analysis.

The software upgrades were compared in two's by applying a Kolmogorov-Smirnov (K-S) test to all the perfusion parameters measured for the 6 CT perfusion studies. The output parameters of a K-S test are the statistic, called D, and it's significance level (Prob). The D statistic represents the maximum vertical deviation between the cumulative distribution functions (CDFs) of the compared datasets. The CDFs are expressed in a fractional way and thus D ranges between 0 and 1, with low values meaning that the CDFs are similar, while large numbers indicate strong discrepancies. The Prob parameter ranges between 0 and 1 as well, and a small value shows that the two CDFs are significantly different. To assess the agreement of two measurements of the same quantity performed with two versions of the software, it is necessary to interpret properly the output of the K-S test, i.e. to combine the D and Prob parameters. For example, if D is significantly lower than 0.5 and Prob larger than at least few percent, then the two software versions under exam give consistent values of that perfusion parameter. On the contrary, when D>0.5 (significantly) and Prob<0.1% the compared versions give discrepant results. Intermediate values of the K-S statistic (e.g. D~0.5) together with Prob~0.1%, correspond to a marginal agreement between the software versions on the perfusion parameter value.

To verify the stability of the three software versions and their reliability we investigated, for each of the 6 CT perfusion studies, the variation of all the perfusion parameters (MTT, BV, BF and PS) against the truncation time (Tt) and computed their standard deviation. Then, we have collected the truncated data in three temporal intervals, chosen in order to maximize the gap in the standard deviations between an interval and it's next.
Table 1: Main features of the 6 CT perfusion studies selected to realize our work. LC = Lung Cancer; HL = Hodgkin Lymphoma; RCC = Renal Cell Carcinoma.

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Results

The output of the K-S test for all the perfusion parameters measured with CT Perfusion 3, 4, and 4D in the 6 CT perfusion studies were shown in **Figures 1-3**.

We stress that the three platforms are always able to process the data.

For each perfusion parameter we have obtained the following results: the CT Perfusion 3 and 4 gave marginally consistent values in 6/24 parameters (the BV and PS for HL2, BV for LC1, MTT for RCC1, BV and PS for RCC2) and significantly consistent values in 5/24 parameters (BF for HL1, BV for LC2, BF and PS for RCC1, MTT for RCC2). The Perfusion 4 and 4D gave marginally consistent parameters in 3/24 cases (BV in HL2, MTT and PS in RCC2) and significantly consistent parameters in 6/24 cases (BV for HL1, MTT, BF and PS in HL2, MTT for RCC1, BF for RCC2).

The Perfusion 3 and 4D gave marginally consistent values in 25% of the parameters (BF and PS for HL1, BV for HL2, PS for LC1, MTT and BF for RCC2) and significantly consistent values in ~17% of the parameters (BV for LC1, PS for RCC1, BV and PS for RCC2). Summarizing, significantly consistent values were found in 15/72 (i.e. ~20%) of the parameters among the entire datasets. Among these, the CT Perfusion 3 and 4 were in agreement in 1 case for the MTT, in 2 cases for the BF, in 1 case for both BV and PS. The CT perfusion 4 versus 4D were in agreement in 2 cases for the MTT, 2 cases for the BF, 1 for the BV and 1 for the PS. Finally, the CT Perfusion 3 and 4D were in agreement never for the MTT and for the BF, in 2 cases for the BV and PS.

The perfusion parameters variation as a function of the truncation time was shown in **Figures 4-9**. In each panel, a visual comparison of the trends for the three software confirms what has been found with the K-S test. The collection of the truncated measurements in three temporal intervals yields the two cuts at 25 and 40 seconds respectively. The total standard deviations and their values in each temporal bin were overplotted in **Figures 4-9**. A standard deviation of 0.00 means that the perfusion parameter remain constant within the truncation interval. In all the CT perfusion studies and for the majority of the parameters, the standard deviation decreases passing from the first interval (Tt < 25 s) to the last one (Tt > 40s). This is deeply discussed in Mazzei et al. (Reduced time CT perfusion acquisitions are sufficient to measure the Permeability Surface area product with a deconvolution method. Oral communication at ECR 2012) and reflects the time needed by the software to reach some stability in the deconvolution algorithm. Beyond this, it is interesting to note that the parameters measured with the CT Perfusion 4D show *always* the lowest standard deviation in all the Tt intervals and also globally. This result demonstrate the higher reliability of the measurements obtained with the CT Perfusion 4D compared with previous versions of the software. In most of the cases (17/24) the largest standard deviation is related to values obtained with the CT Perfusion 4. This happened for both the total standard deviations and the values in the three Tt intervals.
**Fig. 1:** Kolmogorov-Smirnov test. For the six CT perfusion studies, the D statistic and its significance (Prob.) are listed for all the perfusion parameters (MTT, BV, BF, PS) while comparing by two's their CDFs obtained with the three CT perfusion software versions (CT Perfusion 3 vs CT Perfusion 4, CT Perfusion 4 vs CT Perfusion 4D, CT Perfusion 3 vs CT Perfusion 4D). A marginal agreement of the CDFs for a given parameter is highlighted in green, while a significant consistency is showed in purple.

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**Fig. 2:** Kolmogorov-Smirnov test. For the six CT perfusion studies, the D statistic and it's significance (Prob.) are listed for all the perfusion parameters (MTT, BV, BF, PS) while comparing by two's their CDFs obtained with the three CT perfusion software versions (CT Perfusion 3 vs CT Perfusion 4, CT Perfusion 4 vs CT Perfusion 4D, CT Perfusion 3 vs CT Perfusion 4D). A marginal agreement of the CDFs for a given parameter is highlighted in green, while a significant consistency is showed in purple.

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### Fig. 3: Kolmogorov-Smirnov test

For the six CT perfusion studies, the D statistic and its significance (Prob.) are listed for all the perfusion parameters (MTT, BV, BF, PS) while comparing by two’s their CDFs obtained with the three CT perfusion software versions (CT Perfusion 3 vs CT Perfusion 4, CT Perfusion 4 vs CT Perfusion 4D, CT Perfusion 3 vs CT Perfusion 4D). A marginal agreement of the CDFs for a given parameter is highlighted in green, while a significant consistency is showed in purple.

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Fig. 4: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dasched blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds indentify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Fig. 5: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dasch blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds indentify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Fig. 6: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dasched blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds indentify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Fig. 7: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dashd blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds identify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Fig. 8: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dasched blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds identify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Fig. 9: The variation of the truncated perfusion parameters as a function of the truncation time are shown for the six CT perfusion studies (HL1, HL2, LC1, LC2, RCC1, RCC2). Each panel shows the trend of a given perfusion parameter (MTT, BV, BF, PS) measured with the three CT Perfusion software versions: CT Perfusion 3 (dot-dashed green line), CT Perfusion 4 (dasched blue line), CT Perfusion 4D (continuous red line). The dotted vertical lines at 25 seconds and 40 seconds indentify the three temporal intervals where the data are collected. In each interval the measured standard deviations are listed using the above color code. The labels list the total standard deviation as measured with the three software versions: #3, #4 and #4D respectively.

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Conclusion

CT Perfusion version 3.0 vs version 4.0: global consistent results only for RCCs. Perfusion version 4.0 vs version 4D: globally consistent perfusion values in HL2 and RCC2. Perfusion version 3.0 vs version 4D: globally consistent perfusion values RCC2.

The differences between the three versions are possibly due to the introduction of the T0 parameter in the CT Perfusion 4 version and the treatment of the noise applied in the CT Perfusion 4D, as stated by the vendor, even though we can not verify this.

Notably, the agreement in perfusion measurements with different versions of the CT Perfusion software were found in a peculiar compartment like the kidney and in the necrotic tissue (HL2, inactive). This happens because in both cases it is difficult to assess a reliable perfusion: in the first case because the compartmental model adopted to describe the perfusion is too simple to be applied at a complex compartment like the kidney, while in the second case the necrosis does not allow the flow of the contrast. We thus deduce that from the algorithm point of view, the software is measuring just noise.

The CT perfusion 4D tends to have a stable deconvolution algorithm providing reliable measurements. We thus recommend the use of CT Perfusion 4D in clinical practice.
References


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