Impact of low-dose CT scan in dual timepoint investigations: a phantom study

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Abstract. Dual timepoint FDG uptake investigations have a potential for separating malignant lymph nodes from non-malignant in certain cases of suspected lung cancer. One hour seems to be the optimal time interval between the two scans (50-120 min). Many of the new PET scanners benefit from image fusion with a CT image and also use the CT for attenuation correction. In any practical hospital setting, 1 hour is too long to occupy the scanner bed and a second CT procedure thus becomes necessary. This study tries to validate to what extent the dose/quality of the second CT scan can be lowered, without compromising attenuation correction, lesion detection and quantification. Using a standard NEMA phantom with the GE Discovery PET/CT scanner, taken in and out between scan sessions, we have tried to find the minimal CT dose necessary for the second scan while still reaching tissue activity quantification within predetermined error limits. For a hot sphere to background activity concentration ratio of 1:5, the average uptake (normalised by the time corrected input activity concentration) in a sphere of 6 cm³ was found to be 0.90 ± 0.08 for the standard scan, yielding a dose of 5.5 mGy, and 0.90 ± 0.14 for a scan with lowest possible mAs product and lowest possible kV, yielding a dose of 0.65 mGy. With an insignificant increase in the uncertainty in the uptake measurement, we can get an order of magnitude reduction for the CT dose.

1. Introduction

While it is important to aspire toward as accurate diagnostics as possible, the benefits must be weighed against the potential hazards to patients and the costs it might impose. Dual timepoint FDG uptake investigations have a potential for separating malignant lymph nodes from non-malignant in certain cases of suspected lung cancer [1-3]. To detect a change in the FDG uptake of a lesion in two different scans, we must ensure that the uncertainty in a single measurement is smaller than the change we observe. This is done by eliminating or minimising any differences between the two scans. An optimal procedure would be to have the patient lying on the scanner bed - completely still - for the whole duration (scan-pause-scan). This would also have the benefit that the same CT scan could be used for the attenuation correction map for both scans, and the patient only receives the CT dose once. However, while patients referred for a lung PET scan are often quite uncomfortable and weak, lying completely still for 1 hour for each of the two scans, is not realistic. On the cost/benefit side, a small hospital with one PET scanner would have to drastically reduce the number of patients per day, if one procedure lasts 1.5 hours rather than 20 min in the scanner. So realistic implementation of a second
PET scan as a standard tool for diagnosing lung cancer would require a second CT scan, with the extra radiation dose to the patient this entails.

Current software has automated features that are capable of defining a boundary around lesions (areas of higher activity) and to determine the lesion uptake. This was used for volume detection as well as uptake determination.

The sole purpose of this study is to investigate if there is a significant effect on the uptake values found in a lesion in the PET reconstructed images, when different parameters for the CT scan are used for the attenuation map.

2. Materials and methods

The current phantom study was performed on a GE Discovery VCT 64 PET/CT scanner and data processing were carried out on a GE Advantage Workstation running SW version 4.4. The phantom was a standard NEMA phantom with 6 sphere inserts of various sizes. The overall phantom volume is 9.7 litres. “Hot” spheres and phantom background were loaded with known, activity calibrated F-18 solutions, prior to the scans. In between dual timepoint measurements, the phantom was kept stationary on the scanner bed. The scanner software was used to quantify volumes, average and max uptake values (kBq/ml) in that volume. Measured uptake values were compared to the correct values derived from the activity concentrations loaded into the phantom. The ratio between measured and calculated activity is used as a figure of merit and expressed as “correctness” (S). An S value of exactly 1 corresponds to a completely correct measurement. As scans and quantifications were repeated on a given phantom, embracing different activity levels due to decay, several S value determinations were performed for each sphere. For a dataset of such repeated determinations, the mean value, the standard deviation SD and the relative uncertainty RU (SD over mean) were calculated.

The aim of the study is to identify the impact of the CT dose on the correctness. However an initial series of experiments were performed to stage the relevance of this. In preparation, a series of runs were made. First the effect of “lesion” to “background” activity concentration ratio was investigated [5], and then the effect of “lesion” volume [4]. Neither should have an effect in a dual timepoint study, but will set a limit when intrinsic fluctuations become too large to trust a comparison between two measurements. The result from these studies showed a strong dependence but there is no simple way to define lower limits. As a reasonable baseline for this investigation, a signal to noise ratio of approximately 1:5 was chosen and a volume of 5.57 cm³ was used for standard investigations to disregard volume effects. Few investigations with a 0.52 cm³ volume were also conducted. For our purpose, these settings are in agreement with other studies [4, 5].

Second the dose was lowered successively by tuning the noise index, the mAs and the voltages. This was done to reveal any obvious bias or trends in the noise. Even though, there is some variability in the result (data not shown), it was not possible to deduce if these were tied to the quality of the CT scan or just intrinsic variations in the PET data. Thus, the next natural step was a more thorough comparison between two fixed sets of parameters, one that represented a standard patient scan (first scan, 120 kV and smartAmp feature) and a second set of parameters where we chose the lowest possible values (50 mAs and 80 kV). This change in parameters reduced the calculated CT dose to the phantom by a factor 8.4, from 5.47 to 0.65 mGy. The settings are referred as High Dose (HD) and Low Dose (LD).

To avoid bias on the datasets from decay, scans were made alternating between the two sets of parameters. An overview of these results from two different days can be seen in figure 1 and table 1.

3. Results

By far the largest uncertainties showed up in the recovery of the volume (data not shown). However, the uncertainty in the recovery of the uptake value is much smaller and it is surmised that a consistent determination of activity in a lesion can be made without demanding the same precision in volume detection.
In figure 1, the average correctness values are close to one, but with a tendency for deviations in activity concentration levels of 2 kBq/ml and below. This tendency is observed in both the HD and LD datasets and thus is not caused by the change in CT settings.

In table 1, the mean and standard deviation of the correctness value for all datasets as well as a combined set of HD and LD are shown. If there is a shift in the mean between the LD and the HD datasets, we expect to observe a remarkable increase in the relative uncertainty of the combined (HD+LD) dataset. If the datasets dose have the same mean, the relative uncertainty becomes roughly: \(0.5 \left( \sigma_{\text{HD}}^2 + \sigma_{\text{LD}}^2 \right)\). Hence, if the combined dataset has a relative uncertainty between the corresponding relative uncertainties of the individual sets, this means that the datasets are comparable. This is obvious for dataset 1 (table 1), but not so for dataset 2. To elaborate on this result, the relative differences between the means of the LD and HD correctness of the datasets were calculated and compared with the smallest relative uncertainty of the two sets, as shown in table 2. This gives a slightly more positive indication as the relative difference in the mean is quite small and even smaller than or comparable to the smallest fluctuation. Note that for all values, except the average value of the second dataset, HD has the smallest uncertainty.

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\sigma_{\text{avg}} = 0.5 \left( \sigma_{\text{HD}}^2 + \sigma_{\text{LD}}^2 \right)
\]

The relative uncertainty is around 10% for the 5.57 cm\(^3\) volume with a tendency to be slightly larger for the LD dataset. The small volume gives rise to a much larger relative uncertainty (~20%). This is important since the relative uncertainty will set a limit to the acceptance of an important value.

### Table 1.
The number of scans (N), the volume of spheres (V), the mean of the correctness value (S), uptake/input activity concentration in sphere, with the relative uncertainties.

| Dataset 1: First scan activity ~ 2 kBq/ml, last scan activity ~ 0.7 kBq/ml, signal to noise ratio was 1:4.79 |
|---|---|---|---|---|---|
| N | V (cm\(^3\)) | \(\langle S_{\text{max}} \rangle\) | \(\sigma_{\text{max}} / \langle S_{\text{max}} \rangle\) % | \(S_{\text{avg}}\) | \(\sigma_{\text{avg}} / \langle S_{\text{avg}} \rangle\) % |
| HD \(^a\) | 6 | 5.57 | 1.53 ± 0.18 | 11.9 | 0.90 ± 0.08 | 8.7 |
| LD \(^b\) | 6 | 5.57 | 1.49 ± 0.22 | 14.5 | 0.90 ± 0.14 | 15.4 |
| Mixed \(^c\) | 12 | 5.57 | 1.51 ± 0.19 | 12.7 | 0.90 ± 0.11 | 11.9 |

| Dataset 2: First scan activity ~ 4 kBq/ml, last scan activity ~ 1.1 kBq/ml, signal to noise ratio 1:4.77 |
|---|---|---|---|
| HD | 10 | 0.52 | 0.86 ± 0.15 | 18 | 0.53 ± 0.10 | 19.7 |
| LD | 10 | 0.52 | 0.90 ± 0.16 | 17.2 | 0.55 ± 0.13 | 23.9 |
| Mixed | 20 | 0.52 | 0.87 ± 0.15 | 17.2 | 0.53 ± 0.11 | 21.6 |
| HD | 10 | 5.57 | 1.68 ± 0.13 | 7.8 | 1.09 ± 0.09 | 8.2 |
| LD | 10 | 5.57 | 1.81 ± 0.19 | 10.5 | 1.15 ± 0.08 | 6.6 |
| Mixed | 20 | 5.57 | 1.78 ± 0.20 | 11.1 | 1.14 ± 0.09 | 8.3 |

\(^a\) High Dose
\(^b\) Low Dose
\(^c\) Combination of LD and HD

Figure 1: Average correctness value (S) as a function of the input activity concentration in a sphere of 5.57 cm\(^3\). The 4 datasets are: the two different days (D1, D2) and the two CT parameter settings yielding Low Dose (LD) and High Dose (HD).
increase in lesion. Other studies have suggested 2 ml as a minimal volume for accurate uptake measurement [5].

Table 2. The relative difference, $\text{RF} = (\langle S_{\text{HD}} \rangle - \langle S_{\text{LD}} \rangle) / \langle S_{\text{HD}} \rangle$, between the mean 
$S$ values of the LD and HD for the two datasets (D1 and D2) and the smallest 
relative uncertainties (RU).

|       | D1 |     | D2 |     |
|-------|----|-----|----|-----|
|       | RF % | RU % | RF % | RU % |
| Av.   | 0.7 | 8.7 | 6.9 | 6.6 |
| Max.  | 2.3 | 11.9| 5.0 | 7.8 |

4. Conclusion and discussion
The aim of this study has been to uncover any change or bias in correct retrieval of uptake values between two scans that differ only by a change in the parameters for the CT scan used for attenuation correction. Under the assumptions of the performed experiments, the conclusion is that there is no clinically important difference. The results do reveal generally large fluctuations within the datasets, and these should be used to help in determining how much the uptake needs to change before we consider any change significant. With a lesion activity concentration of 4 kBq/ml or less and a background to noise ratio of roughly 1:5 any change less than 10% can not be considered significant.

In the actual human scanning situation, with more scatter, repositioning problems and movements, the limits to what can be considered significant is probably even higher.

The average and maximum values are fairly consistent; although the variability is lower in the average values. The relative uncertainty in the average uptake in the large sphere is 10%, so in this case increases in uptake of more than 10% could be detected with certainty. Initial patient studies on site have shown a tendency for the investigated lesions to have quite a large relative increase in uptake. Thus, at present 41 lesions from 17 consecutive patients have been investigated and for these, 70% (± 14%, 95% confidence) had an increased uptake of more than 10% (with the second scan on average 85 ± 6 min after the first). None of these lesions have yet been verified or rejected as malignant, but they reveal that a large quantity of the data we work with, have an increase in uptake that is significant (e.g. above 10%). Other studies show similar tendencies [1], 20 malignant lesions showed an average increase of 20.5%, which in our study would be considered adequate. Lesion sizes were not considered for these data.

The conclusion concerning a lower boundary for the significance is only valid in the case of a well calibrated scanner. If the dual timepoint method was implemented as standard procedure, it would be advisable to test this as a part of the standard QA. In this study, we used two different voltage settings for the HD and LD scans, from 120 kV to 80 kV. By only changing the mAs and maintaining the same kV the dose will increase (to 1.7 mGy); any possible systematic errors have been removed.

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