Bioimpedance-based respiratory gating method for oncologic positron emission tomography (PET) imaging with first clinical results

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Abstract. Respiratory motion may cause significant image artefacts in positron emission tomography/computed tomography (PET/CT) imaging. This study introduces a new bioimpedance-based gating method for minimizing respiratory artefacts. The method was studied in 12 oncologic patients by evaluating the following three parameters: maximum metabolic activity of radiopharmaceutical accumulations, the size of these targets as well as their target-to-background ratio. The bioimpedance-gated images were compared with non-gated images and images that were gated with a reference method, chest wall motion monitoring by infrared camera. The bioimpedance method showed clear improvement as increased metabolic activity and decreased target volume compared to non-gated images and produced consistent results with the reference method. Thus, the method may have great potential in the future of respiratory gating in nuclear medicine imaging.

1. Introduction

Positron emission tomography (PET) combined with computed tomography (CT) imaging is an important tool in oncology. Studies with fluorine 18 ([¹⁸F]) –based radiopharmaceuticals can be used for cancer staging and treatment response evaluation, for example [1]. Respiratory motion is a significant error source in PET/CT studies of thoracic region. Due to the long imaging time of PET, which is typically minutes, respiratory motion leads to image blurring, which may result in overestimation of target’s size and underestimation of its metabolic activity [1].

At present, there are many studies on minimizing motion artefacts by synchronizing, or gating, the image reconstruction with a simultaneously recorded respiratory signal. The respiratory signal is most often derived from thoracic or abdominal chest wall motion, which is typically monitored by infrared camera or pressure belt [1, 2]. However, respiratory gating has been adopted slowly in clinical routine. One reason for this may be that the methods have been considered complicated and cumbersome to use.

Our aim is to develop a bioimpedance-based respiratory gating method, which is as accurate as previously introduced respiratory gating methods but easier and faster to use. Previously, an optimized four-electrode bioimpedance measurement configuration was determined horizontally on anterior upper thorax using sensitivity analysis and volunteer measurements [3]. Further, high correlation and
very good agreement was confirmed between respiratory bioimpedance measurements and reference spirometer measurements in healthy volunteers [4]. The aim of this paper is to compare developed bioimpedance gating method with a widely studied reference method and to show that the results are consistent between the methods.

2. Methods

Twelve oncologic patients (4 women, 8 men) were recruited to this study in Turku PET Centre. The patients’ age was 46-77 (mean 65) years and their body mass index varied in the range of 21.3-38.5 (mean 26.3) kg/m². The gating study was conducted alongside the clinical PET/CT study, to which the patients were referred. Written informed consent was obtained from all of the patients and the study was approved by the ethical committee of Kuopio University Hospital (Dnro 90/2011).

The PET/CT imaging was performed with a high-resolution Discovery 690 PET/CT scanner (GE Medical Systems, Milwaukee, USA) and [18F]-labeled radiopharmaceuticals ([18F]-fluorodeoxyglucose, [18F]-FDG or [18F]-fluorodihydroxyphenylalanine, [18F]-FDOPA). The bioimpedance measurement was carried out with EBI100C bioimpedance amplifier (Biopac, Goleta, USA) and processed in MATLAB R2007B (MathWorks Inc., Natick, USA). The processing of bioimpedance measurement consisted of the removal of cardiac component from the band between 0.6-20 Hz using 5th order Butterworth filters and smoothing of the remaining respiratory signal with moving average filter of 100 ms. If a clearly non-physiological drift was observed in the signal, a 50 s moving average filter was additionally applied for detrending. Real-time Position Management (RPM) system (Varian, Palo Alto, USA) was used as reference gating system in the study. The gated image reconstruction was performed with GE Research Gating Tool (RGT) based on breathing depth. Thus, only PET data during end-expiration, which was considered the longest and most stable phase of respiration, was included in the image reconstruction. In this study, end-expiration was determined as the lowest fifth of the respiratory amplitude of each cycle individually (figure 1). Due to excluding large part of the PET data in the gating process, the PET imaging time was increased to 10 minutes compared to 2 minutes used in the non-gated study. An averaged CT over the whole respiratory cycle was used for the attenuation correction of the PET data.

Figure 1. Selection of end-expiratory periods from the respiratory bioimpedance measurement for the reconstruction of PET image. Horizontal lines illustrate the amplitude limits (the lowest fifth of the respiratory amplitude) that determine the boundaries of end-expiratory periods in time. End-expiratory periods are depicted by dashed vertical lines.

Three image sets of each patient were created in the study: standard non-gated, bioimpedance-gated and RPM-gated. The bioimpedance gating method was evaluated by studying the difference and correlation of three parameters between bioimpedance- and RPM-gated images as well as the change of these parameters compared to non-gated images. The studied parameters were maximum metabolic...
activity of the target, observed target size and target-to-background ratio. The parameters were determined with standard clinical AW Workstation 4.5 (GE Medical Systems, Milwaukee, USA). The targets were delineated utilizing the volume of interest (VOI) tool. Maximum metabolic activity (g/ml) was determined as the maximum voxel value in the target. The target size was determined as the volume of the target (cm$^3$), where the activity of the target was 50-70 % of its maximum activity. The threshold varied slightly between the patients in order to achieve reliable delineation of the target in all image sets. Target-to-background ratio was determined as the ratio of mean metabolic activity in the observed target volume and mean of background activity within VOI, which was determined on the flank of the patient with no specific uptake of the radiopharmaceutical.

3. Results

The radiopharmaceutical uptake of the target is more visible in both gated images compared to the non-gated image (figure 2). The maximum metabolic activity was determined in altogether 15 targets in 11 patients. The targets of one patient were excluded from the analysis, since no averaged attenuation correction CT was available. The maximum metabolic activity changed -6.3 - +122.4 % (mean 20.5 ± 31.5 %) from non-gated to bioimpedance-gated images, whereas with the RPM-gated images the corresponding range was 1.6-104.1 % (mean 20.6 ± 26.1 %). On average, the maximum metabolic activity between bioimpedance and RPM gating differed 3.8 ± 3.8 % (of the RPM-based measurement). The correlation of maximum metabolic activity measurements of gated images was very high ($R^2 = 0.978$) (figure 3a).

![Figure 2](image_url)

Figure 2. The radiopharmaceutical accumulation of the target (pointed by the arrow) in non-gated (a), bioimpedance-gated (b) and RPM-gated (c) transaxial image. The PET image is fused with the CT image. In each case (a, b, c) the slice with the most distinguishable target is shown.

The target size was observed from 13 targets in 9 patients. Two additional patients were excluded in this analysis, due to the complicated form of the target, for which it was not possible to delineate the volume of the target reliably. Compared to non-gated images, the target size changed -62.0 - +16.4 % (mean -18.0 ± 25.5 %) in bioimpedance-gated images and -63.9 - +27.4 % (mean -16.0 ± 25.6 %) in RPM-gated images having the average difference of 8.2 ± 5.7 % between gated images. Furthermore, a very good correlation ($R^2 = 0.954$) was observed between the gating methods (figure 3b).

Target-to-background ratio was determined from the same targets as the size, since the observed target size essentially affects the mean metabolic activity value, which is used in calculating the target-to-background ratio. Target-to-background ratio increased from the non-gated to bioimpedance- and RPM-gated images by -4.8 - +132.3 % (mean 22.7 ± 36.9 %) and 0.0-116.1 % (mean 21.1 ± 32.4 %), respectively. The mean difference between the gating methods was 2.4 ± 2.8 % and the measurements correlated excellently ($R^2 = 0.994$) with each other (figure 3c).
4. Discussion and Conclusion

As expected, both gating methods compensate effectively the overestimation of target size and the underestimation of the metabolic activity of the target. The increase of target-to-background ratio was also expected. In addition, the measurements of all three parameters are consistent between bioimpedance and RPM gating and have a very high correlation. The mean differences between the bioimpedance- and RPM-gated measurements are small in all studied parameters, though the range of measurement results is considerably wide. Comparing the means of the measured change in parameters between non-gated and gated image sets, bioimpedance gating has a slightly stronger effect on parameters than the RPM method. However, more patient studies are required for a definite conclusion on the relation between bioimpedance and RPM gating.

The results of this study show that bioimpedance-based respiratory gating produces consistent results in oncologic PET/CT studies with the widely used RPM method. Moreover, the bioimpedance method is very straightforward and fast for the technologists to use. Thus, the method may have great potential in the future of respiratory gating in nuclear medicine imaging.

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References

[1] Nehmeh S A, Erdi Y E, Clifton C L, Rosenzweig K E, Schoder H, Larson S M, Macapinlac H A, Squire O D and Humm J L A reference 2002 Effects of respiratory gating on quantifying PET images of lung cancer. J. Nucl. Med. 43 876-81

[2] Bundschuh R A, Martínez-Möller A, Essler M, Martínez M-J, Nekolla S G, Ziegler S I and Schwaiger M 2007 Postacquisition detection of tumor motion in the upper abdomen using list-mode PET data: a feasibility study J. Nucl. Med. 48 758-63

[3] Koivumäki T, Vauhkonen M, Kuikka J T and Hakulinen M A 2011 Optimizing bioimpedance measurement configuration for dual-gated nuclear medicine imaging: a sensitivity study Med. Biol. Eng. Comput. 49 783-91

[4] Koivumäki T, Vauhkonen M, Kuikka J T and Hakulinen M A 2012 Bioimpedance-based measurement method for simultaneous acquisition of respiratory and cardiac gating signals Physiol. Meas. 33 1323-34