



SAHLGRENSKA ACADEMY

HOW IMAGE QUALITY IS AFFECTED BY A NON-OPTIMAL COUNT RATIO BETWEEN VENTILATION AND PERFUSION WHEN PERFORMING V/P SPECT

- OPTIMIZATION OF V/P SPECT QUOTIENT IMAGE QUALITY

Master's Thesis

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Supervisors:	Johanna Dalmo, Jacob Himmelman and Jehangir Khan
Examiner:	Magnus Båth

Abstract

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Purpose: The main purpose with this study was to evaluate how image quality is affected when performing ventilation/perfusion single photon emission computed tomography (V/P_{SPECT}) studies whilst using non-optimal ventilation/perfusion count ratios due to a high variance in patient technegas inhalation. Furthermore, the current choice of equipment and parameter values used at Sahlgrenska University Hospital (SU) was evaluated and optimized for using a low energy, high resolution (LEHR) collimator instead of the recommended low energy, general purpose (LEGP) collimator.

Theory: Lung scintigraphy is widely considered as the go-to imaging technique for accurately diagnosing pulmonary embolism. In modern times, the more sophisticated V/P_{SPECT} has been replacing the static ventilation/perfusion planar scintigraphy (V/P_{PLANAR}) by introducing the possibility to acquire images from multiple angles. V/P_{SPECT} also has a higher sensitivity/specificity compared to other imaging techniques such as computed tomography of the pulmonary arteries (CTPA). Today's guidelines, presented by the European association of nuclear medicine (EANM), suggest that a 3 to 1 perfusion/ventilation count ratio is the optimal choice to achieve the lowest relative noise levels in the V/P quotient image Q while using a LEGP collimator. The administered perfusion dose can be administered with minimum variance, but the patients' ability to inhale the desired amount of ventilation activity varies. This often causes non-optimal count ratios and may affect the resulting image quality.

Method: A MATLAB script was created that was based on the current mathematical methods used to evaluate V/P_{SPECT} quotient image quality through calculation of relative standard deviation (i.e. relative noise levels). The reliability of the completed script was validated by comparing calculated noise levels with values compiled through phantom study while using the same parameter values. $N = 37$ clinical V/P_{SPECT} studies made at SU were evaluated and an average ventilation & perfusion count rate was compiled. Since SU uses a LEHR collimator instead of the EANM recommended LEGP collimator the current perfusion count rates are lower than what is recommended due to no parameter value compensations being made. The MATLAB script was used to compile new parameter combinations to lower the current noise levels to what are considered standard. The script was then used to calculate how different ventilation count rates and perfusion/ventilation count rate ratios R_p/R_v are affecting image quality.

Results: The reliability of using the MATLAB script was validated when compared to the phantom studies using matching parameter values. The average perfusion count rate acquired at SU is on average 38% lower than what is recommended by EANM due to using a LEHR collimator instead of the recommended LEGP collimator. The validated MATLAB script was used to compile a total of 8 parameter combinations with an increased perfusion count rate, acquisition time or a combination of both. Each combination resulted in the same relative noise level as when using a recommended EANM guideline values. In conclusion, the impact of the R_p/R_v ratio on the image quality is very low when performing V/P_{SPECT} . Instead, resulting image quality depends heavily on obtained perfusion image count rate and acquisition time distribution.

Populärvetenskaplig sammanfattning

Bakgrund

Människans lungor kan delas upp i mindre segment som får sin genomblödning (perfusion) från varsin dedikerad artär. Lungemboli är ett tillstånd som uppkommer då en eller flera blodproppar fastnar i en av segmentens artärer och blockerar segmentets perfusionsförmåga. I många fall leder detta till akuta tillstånd. Det är därför viktigt att man snabbt och effektivt kan ställa diagnos för att öka chansen till full återhämtning.

En av de mest pålitliga bildtagningarna för att ställa diagnos är tredimensionell lungscintigrafi, mer känt som V/P_{SPECT} . Denna undersökning kartlägger lungornas ventilations- och perfusionsförmåga. Patienten får andas in en radioaktiv gas och en bildtagning med en gammakamera utförs av lungorna. Därefter injiceras ett radioaktivt spårämne till patientens blodström som tas upp i lungornas kapillärer och en perfusionsbildtagning utförs på samma sätt som tidigare. Bilderna jämförs sedan genom att dividera ventilations- och perfusionsbilderna och skapa så kallade kvotbilder. Om ett eller flera lungsegment har nedsatt genomblödning men bibehållen ventilation så kan lungemboli konstateras. För att utföra bra diagnostik behöver bilderna gå att skilja från varandra.

På SU använder man en mer högupplöst kollimator än vad som rekommenderas enligt riktlinjerna. Detta medför att den aktivitetskvot som föreslås mellan ventilation och perfusion inte är optimal och behöver ses över. Erhållen ventilationsaktivitet baseras på patientens inandningsförmåga – något som varierar med patientens allmäntillstånd.

Mål

Huvudmålet med arbetet var att undersöka hur en varierad ventilationsaktivitet påverkar brusnivåer i kvotbilder. Eftersom perfusionsaktivitet och insamlingstider inte har korrigerats för den högupplösta kollimator som används på SU, så undersöktes nya parametrar för SU som kompenserar för detta. Ett MATLAB-skript togs fram för att matematiskt beräkna kvotbildskvalitet.

Resultat

Resultaten visar att bildkvaliteten i V/P_{SPECT} -kvotbilder endast påverkas marginellt då icke-optimala aktivitetskvoter erhålles till följd av varierande ventilationsaktivitet. Endast vid mycket låg ventilationsaktivitet sker en kraftig ökning av brus i kvotbilden. Det som huvudsakligen påverkar bildkvaliteten är istället administrerad perfusionsaktivitet och fördelning av insamlingstider. Vidare togs nya parameterkombinationer fram för kompenserande av den högupplösta kollimator som används på SU.

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Abbreviations

COPD	Chronic obstructive pulmonary disease
CTPA	Computed tomography of the pulmonary arteries
EANM	European association of nuclear medicine
KU	Karolinska University Hospital
LEGP	Low energy, general purpose
LEHR	Low energy, high resolution
MAA	Macroaggregated albumin
OSEM	Ordered subset expectation maximization
PE	Pulmonary embolism
PH	Pulmonary hypertension
RSD	Relative standard deviation
ROI	Region of interest
STDEV	Standard deviation
SU	Sahlgrenska University Hospital
V/P _{SPECT}	Ventilation/perfusion single photon emission computed tomography
V/P _{PLANAR}	Ventilation/perfusion planar scintigraphy

1 Introduction / Aim

1.1 Introduction

The field of nuclear medicine is diverse and many patients are being diagnosed through different imaging studies every year. One examination that is particularly effective for proper diagnosis is ventilation/perfusion single photon emission computed tomography (V/P_{SPECT}) [1-2]. The main purpose of this examination is to diagnose pulmonary embolism (PE) - a treatable illness where a thrombus blocks the perfusion in the lungs [3]. As PE often causes an acute state, proper diagnosis is preferred to be made within 24 hours of incidence [4-5]. Compared to other imaging techniques, V/P_{SPECT} currently is one of the most accurate for diagnosing PE regarding sensitivity/specificity [4,6-7]. The examination involves two acquisitions where images of the patients' pulmonary ventilation (V) and perfusion (P) are compared by creating a quotient image (Q). Administered $^{99\text{m}}\text{Tc}$ activity is inhaled and injected intravenously prior the ventilation and perfusion examination respectively [1-2,5].

There are four main parameters that determine the resulting image quality: ventilation and perfusion count rate (R_v and R_p) and ventilation and perfusion acquisition time/angle (T_v and T_p) [2]. Current guidelines presented by the European association of nuclear medicine (EANM) states that a count ratio $R_p/R_v=3$ and time ratio $T_p/T_v=0.5$ will result in the least amount of noise in quotient image Q while using a low energy, general purpose (LEGP) collimator [1]. Due to difference in physical states, patient inhalation capacity varies heavily throughout, often resulting in non-optimal count ratios [2].

1.2 Aim

The aim with this study was to develop a method to see how V/P_{SPECT} quotient image quality is affected when using non-optimal ventilation/perfusion count ratios due to varying patient inhalation capacity. Furthermore, an extensive evaluation and optimization of current parameter values used at Sahlgrenska University Hospital (SU) was made as they use a low energy, high resolution (LEHR) collimator instead of the recommended LEGP collimator.

2 Theory

2.1 V/P_{SPECT} – an introduction

V/P_{SPECT} is a non-invasive technique to examine lung functions. The main focus of a V/P_{SPECT} examination is to review the relation between pulmonary ventilation and perfusion. It is widely used for the diagnosis of many lung diseases, including PE [1-2]. In case of PE, a thrombus blocks the pulmonary perfusion to one or more of the lungs' sub-segments. The thrombus usually migrates from other parts of the body, often originating from the lower extremities. There are many factors causing the thrombus to form, including obesity, smoking and certain cancers [3]. *Figure 1* demonstrates the segments of the lungs being affected by PE as their respective single-end artery is blocked [1]. Accurate diagnosis at an early stage can increase patient life expectancy and should preferably be made within 24 hours of incidence [4-5]. As compared to diagnosis sensitivity, high specificity is also preferred as resulting treatment methods may cause further trauma to the patient [1].

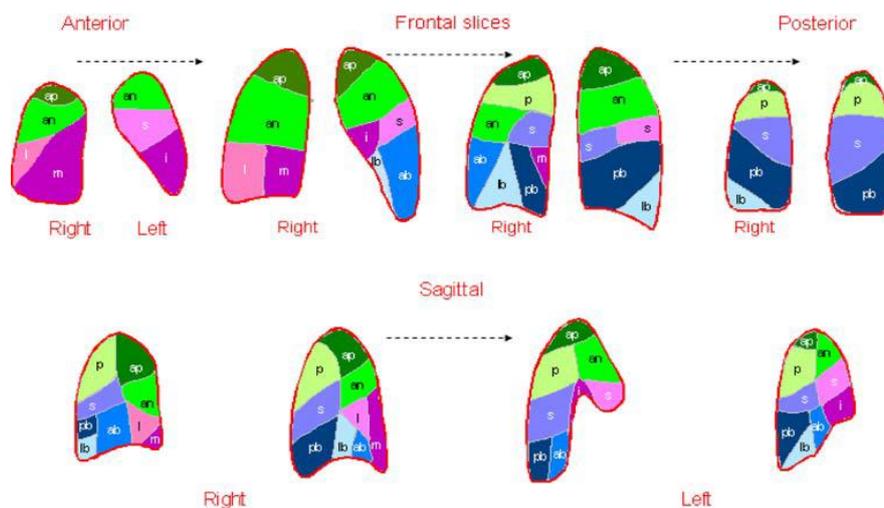


Figure 1: Demonstration of sub-segmental anatomy of the lungs. Every segment is supplied by a single-end artery, resulting in the whole segment being affected if PE disrupts the respective artery. The shape and placement of each segment plays a key role when diagnosing PE through V/P_{SPECT} imaging. Image is adapted from *Bajc et al. (2009)* [1]

The best way of properly diagnosing PE is through different imaging techniques. Several studies show that V/P_{SPECT} result in higher diagnosis sensitivity/specificity when compared to other techniques, often suggesting that it is currently the best choice for PE diagnosis [4,6-7]. Other techniques include computed tomography of the pulmonary arteries (CTPA) and ventilation/perfusion planar scintigraphy (V/P_{PLANAR}) – an older, static version of V/P_{SPECT} [4]. Compared to CTPA, V/P_{SPECT} patients also receive a lower effective dose, and there is no risk of eventual allergic complications due to the contrast fluids that are used when performing CTPA [1,8].

2.2 Performing a V/P_{SPECT} examination

A V/P_{SPECT} examination is divided into three parts:

1. **Ventilation tomography**
2. **Perfusion tomography**
3. **Presentation of V/P_{SPECT}**

Procedure to perform ventilation tomography

During the first part of the examination, the patient inhales a gas containing graphite particles labelled with the radioactive isotope ^{99m}Tc (technegas). The sizes of the hydrophobic graphite particles (0.005-0.2 μm) results in homogeneous distribution throughout the lung alveoli [1]. The technegas is inhaled in a supine position in order to reduce the naturally occurring gradient of ventilation distribution in the lungs [2]. During the inhalation the resulting count rate is monitored and inhalation is stopped when a suffice count rate has been obtained [5]. The physical state of the patient heavily affects the resulting count rate, and for very sick patients it can sometimes be difficult to achieve the desired count rate [2]. After the inhalation the patient is directly transferred to a gamma camera and a ventilation tomography (V) is performed [2]. A dual-headed gamma camera is often used in order to decrease the overall scan time. A typical effective dose (E) to adults from the technegas is $E_{vent} = 0.015$ mSv/MBq (adults) [9].

Procedure to perform perfusion tomography

Ventilation tomography is directly followed by perfusion tomography. During the perfusion examination, the patient is injected intravenously with ^{99m}Tc-macroaggregated albumin (MAA) while still being in a supine position in the camera room [1-2,5]. The size and properties of the MAA particles result in the radioactivity being accumulated in the capillary elements of the lungs. After a successful injection the perfusion tomography is performed [5]. Due to the ventilation examination being directly followed by the perfusion examination, the initial perfusion tomography consists of both perfusion and ventilation activity (known as *ventilation background*). Perfusion-only tomograms (P) are created by subtracting the ventilation background [2,7]. A typical effective dose (E) to adults from ^{99m}Tc-MAA is $E_{perf} = 0.011$ mSv/MBq (adults) [9].

Procedure for presentation of V/P_{SPECT}

The first step is reconstructing tomograms based on the acquisitions from each examination. This is followed by subtraction of ventilation background in initial perfusion tomograms, along with lung delineation and normalization. Normalization equalizes the average pixel value in the reconstructed ventilation (V) and perfusion-only (P) tomograms. Lastly, $Q=V/P$ quotients are created using the normalized ventilation and perfusion-only tomograms [1-2,7].

Quotient images will highlight segments with regular ventilation and low perfusion, called V/P mismatch as shown in *figure 2* [1-2]. V/P mismatch in quotient images can be used to properly diagnose PE.

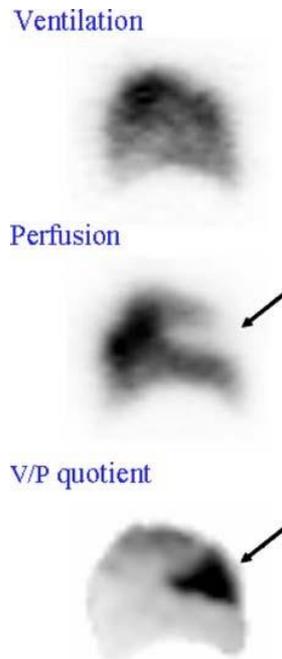


Figure 2: Sagittal slice of a patient's left lung where ventilation tomogram (V), perfusion-only tomogram (P) and V/P quotient Q are depicted based on each tomography. Loss of signal in one of the lung's sub-segments is highlighted the quotient image (wedge-shaped area), indicating pulmonary embolism (PE). Image is adapted from *Bajc et al. (2009)* [1]

2.3 Imaging parameters and protocols

V/P_{SPECT} imaging parameters consist of ventilation and perfusion count rates R_v and R_p , along with set acquisition time per angle T_v and T_p , respectively. Initial perfusion acquisitions are based on the sum of both R_v and R_p . Subtracted ventilation background is weighted by $T_{pv} = T_p/T_v$ to account for possible differences in acquisition time/angle for each acquisition. Patient clearance is not accounted for [2].

Either a LEGP or LEHR collimator is generally used while performing V/P_{SPECT} [1-2,4]. EANM recommends using a LEGP collimator along with a 3 to 1 perfusion/ventilation count rate ratio (i.e. $R_p/R_v = 3$), in order to achieve the least amount of relative noise in Q. Furthermore, the recommended acquisition time per angle during the perfusion examination is half that of the ventilation examination (i.e. $T_p/T_v = 0.5$) for the same purpose [2]. *Table 1* demonstrates equipment and parameter values recommended by EANM [1-2], including administered perfusion and ventilation activities A_{perf} and A_{vent} , along with acquisition time/angle for perfusion and ventilation and T_p and T_v respectively. Recommended values are

based on using a LEGP collimator and a reconstruction matrix size of 64×64 . Recommended ratios and parameter values recommended by EANM are deducted from an examination made by *Palmer et al. (2001)* [2].

Table 1: Parameter values for clinical V/P_{SPECT} studies as recommended by EANM. All recommended values are based on using a LEGP collimator and a reconstruction matrix size of 64×64 . No recommendations regarding energy windowing or zoom factor are mentioned in the guidelines.

Collimator type	LEGP
Reconstruction matrix size	64×64
# of projections	128
A_{vent}	25-30 MBq, Technegas
A_{perf}	100-120 MBq, ^{99m}Tc -MAA
T_v [s]	10
T_p [s]	5

Table 2 shows equipment and parameter values used when performing V/P_{SPECT} at Sahlgrenska University Hospital (SU), according to the current method description [5]. The method includes collimator type, reconstruction matrix size, no. of projections, parameter values including T_p , T_v , A_{perf} , desired R_v , energy window and zoom factor. Theoretical administered ventilation activity A_{vent} due to desired R_v is also included in the table.

Table 2: Parameters used when performing V/P_{SPECT} at SU. Parameters are mainly deducted from the EANM guidelines, except for using a LEHR collimator instead of the recommended LEGP collimator, theoretically resulting in doubled administered ventilation $A_{vent}=50-60$ MBq activity in order to reach the desired count rate of $R_v=2-2.5$ kcps.

Collimator type	LEHR
Reconstruction matrix size	64×64
# of projections	120 (3° /angle, continuous acquisition)
R_v [kcps]	2-2.5
A_{vent}	50-60 MBq, Technegas
A_{perf}	120 MBq, ^{99m}Tc -MAA
T_v [s]	10
T_p [s]	5
Energy window	^{99m}Tc 140 keV ($\pm 10\%$) + scatter 108 keV ($\pm 12.5\%$)
Zoom factor	1.0

2.4 Image reconstruction

Ordered-subset expectation maximization (OSEM) is the recommended reconstruction method, generally using eight subsets and two iterations [2,5]. The software used when compiling the resulting images varies from different institutions. The nuclear medicine specialists at SU mainly use the *HERMES Lung V/Q quantification* software to reconstruct/study the ventilation, perfusion and quotient images [5].

2.5 Criteria for diagnosing PE using V/P_{SPECT}

Interpretation of quotient images should be based on knowledge and experience. Resulting diagnosis of PE (yes/no) is based on whether there is a mismatch of at least one or more of the lungs sub-segments seen in the quotient image [1,10-12]. A mismatch that is not equivalent to a lobar, segmental or sub segmental structure cannot be directly linked to PE and may be caused by other diseases or imaging artefacts due to motion et cetera [4,10].

Other cases where PE can be discarded are when there is a so-called *match* or *reversed mismatch* in the quotient image. A *match* is a segment in Q where there is both an absence in ventilation and perfusion. In such cases, PE can be ruled out as the ventilation is more likely to be the cause of the lack of perfusion. This is one of the reasons why it is important to have both a ventilation and perfusion-only image to reduce the chances of false positive PE diagnosis with no ventilation comparison [1,5]. In cases with *reversed mismatch*, the ventilation element is lacking whilst the perfusion is normal [13]. This naturally does not lead to a PE diagnosis, but instead is a way of discarding PE in the case of dyspnoea (one of the main symptoms of PE).

In the end, if PE is ruled out there is still a chance of diagnosing other pulmonary diseases thanks to V/P_{SPECT} such as lung cancer obstructing the ventilation pathways [14]. The criteria also make it so that proper PE diagnosis may be performed in the presence of other perfusion pejorative diseases such as chronic obstructive pulmonary disease (COPD) and pulmonary hypertension (PH) [1].

3 Method

3.1 MATLAB simulation

In order to mathematically calculate relative standard deviation (i.e. relative noise level) in V/P quotient image Q , a script was created using MATLAB (version R2017b). The script was designed to simulate any scenario using combinations of V/P_{SPECT} parameters T_v , T_p , R_v and R_p . Any mathematical criteria such as maximum acquisition time or maximum acceptable relative noise level could be added by the user. The relative standard deviation in the V/P quotient was calculated using the following equation used in the *Palmer et al. (2001)* study:

$$\frac{\sigma^2(Q)}{Q^2} = \frac{\frac{((R_p+R_v)T_p)^2}{R_vT_v} + (R_p+R_v)T_p}{((R_p+R_v)T_p - T_pR_vT_v)^2} \quad \text{Eq. 1}$$

The function of MATLAB script was validated by using the same criteria as in the study by *Palmer et al. (2001)*, where $T_{tot}=T_p+T_v$ and $R_{tot}=R_p+R_v$ are limited to fixed values. R_p/R_v and T_p/T_v ratios were plotted for a range of parameter values and then compared. The MATLAB script was considered validated if the same optimal time and count ratios were concluded as in the study.

3.2 Phantom study

The reliability of the calculated noise levels acquired from using the MATLAB script were validated through a phantom study. A plastic, cylindrical homogenous phantom filled with water was used to compile a series of quotient images. The relative standard deviation was extracted and compared with calculated values using the MATLAB script when using the same parameter values. The dimensions of the phantom are presented in *table 3*.

Table 3: Specifications of the phantom used when performing the phantom-based study

Type	Cylindrical
Total diameter [cm]	15.5
Compartment diameter [cm]	12
Total height [cm]	20.5
Compartment height [cm]	18

A dual-headed gamma camera (Optima 640, GE Healthcare, Little Chalfont, UK) with a LEHR collimator was used. Specifications of the gamma camera are listed in *table 4*. The cylindrical phantom with a volume of ~2050 ml was filled with a homogenous solution of water and ^{99m}Tc -pertechnetate. For the sake of simplicity, a phantom tomography using either parameters equivalent to ventilation or perfusion studies were named accordingly (i.e. a phantom tomography using ventilation parameter values was labelled as ‘ventilation’). This made it easier to compare values from the phantom study with MATLAB-simulated values.

Table 4: Specifications of the gamma camera system used in the phantom studies

Manufacturer	GE Healthcare
Model name	Optima 640
Collimator type	LEHR
Collimator hole diameter [mm]	1.5
Collimator hole length [mm]	35
Septal thickness [mm]	0.4
Scintillation crystal thickness [mm]	9.5
No. of PM tubes	59
Energy window	^{99m}Tc 140 keV ($\pm 10\%$) + scatter 108 keV ($\pm 12.5\%$)
Zoom factor	1.0

The detector sensitivity of the gamma camera using a LEHR collimator was measured with the phantom in an anterior/posterior (AP/PA) position, i.e. being as close as possible to the anterior-positioned collimator before starting the V/P_{SPECT} acquisition (the same positioning as when performing patient studies). Proper activity administration knowledge to achieve desirable count rates was crucial when determining the detector sensitivity. Before each tomography, the phantom was positioned in the centre of rotation with a starting position of 0 degrees for the corresponding ventilation and perfusion study in order to easily match images from the respective acquisition. The same phantom was used for both the ventilation and perfusion acquisition to match the clinical setting where both perfusion and ventilation activity is present in the initial perfusion tomography.

When performing the phantom V/P_{SPECT} study, the same acquisition protocol as in V/P_{SPECT} studies at SU was used [5]. Before the start of each examination series, the collimators were positioned in their AP/PA position and resulting counts per second (cps) from the phantom in the anteriorly positioned detector was registered.

To review and compile the quotient images for each image collection in the phantom study, the *Xeleris Functional Imaging Workstation 3.1067 (2013, GE Healthcare, Little Chalfont, UK)* was used. The T_p/T_v -weighted ventilation image was subtracted from the initial perfusion acquisition using the *Xeleris’ Arithmetic tool*. A quotient image for each tomography acquisition angle was compiled by dividing the ventilation image with the perfusion-only image. To increase the dynamic range of the pixel resolution windowing tool, the ventilation image was increased by a factor 10^3 before proceeding with the quotient image division. As this

factor increases both the standard deviation and the average pixel count rate in the quotient image, the original relative standard deviation was preserved. After compiling quotient images for each angle, a rectangular-shaped region of interest (ROI) with a pixel area 98 was created and placed inside the overlapping area in each quotient image. The selected area resulted in well-defined margins outside the ROI. Relative standard deviation (RSD) was calculated using the following equation:

$$\text{RSD} = \frac{\text{STDEV}(\text{ROI})}{\text{AVG}\#(\text{ROI})} \quad \text{Eq. 2}$$

STDEV(ROI) represents the image standard deviation and AVG#(ROI) represents the average pixel value in the selected ROI. Each calculated RSD was multiplied by a factor 100 to show it as a percentage. An average estimation and variance yield of the 120 calculated RSD-values for each image acquisition was calculated and registered. The sample standard deviation STDEV was acquired through the ‘n-1’ formula, where x is the current sample, \bar{x} is the calculated mean and n is the sample size:

$$\text{STDEV} = \sqrt{\frac{\sum(x-\bar{x})^2}{(n-1)}} \quad \text{Eq. 3}$$

To reduce the overall amount of phantom studies, an in-house Xeleris-based program *Sim. Reduced Time* was used to simulate different acquisition times. The program uses Poisson resampling and has been validated as a viable alternative to simulate dose distributions.

After several phantom-generated quotient images had been gathered and their respective relative standard deviation registered, each value was plotted and compared to the respective value simulated for the same parameters using the MATLAB script. If the plotted values from MATLAB simulations and phantom study followed the same pattern for both the generated values, the reliability of further using the MATLAB script is confirmed.

3.3 Evaluation of clinical SU parameter values

The *Xeleris* imaging software was used to validate which ventilation and perfusion count rates that are normally received when performing V/P_{SPECT} at SU. The average ventilation and perfusion count rate were noted for $n = 37$ randomly selected clinical V/P_{SPECT} studies. Each extracted value was based on the total number of counts divided by the number of acquisition angles and acquisition time.

To achieve the perfusion-only count rate, the ventilation count rate was subtracted from the mixed ventilation and perfusion count rate in the initial perfusion acquisitions. The mean value was calculated for each parameter and later used when modifying the current parameters used at SU. The sample standard deviation was calculated using the formula presented in Eq. 4. No decay correction was made due to the short period of time in-between each study.

3.4 SU parameter modification and evaluation

To lower the current LEHR-based noise levels in the clinical V/P_{SPECT} images made at SU, parameter values must be modified. With the idea of only changing the parameters and not introduce any image filtering, three main alternatives are available to achieve the same noise levels as using the EANM-guidelines recommended LEGP-collimator:

1. Increase the administrated perfusion dose A_{perf}
2. Increase the administrated perfusion dose A_{perf} and total acquisition time T_{tot}
3. Increase the total acquisition time T_{tot}

Based on the previous evaluation of the clinical V/P_{SPECT} studies ($n=37$), acquired noise levels using the current average perfusion count rate $\bar{R}_{p,\text{SU}}$ were calculated for $R_v=0.5-4.0$ kcps using the validated MATLAB script. A criterion was then implemented only allowing parameter combinations resulting in noise levels within $\pm 1\%$ of the levels received when using the recommended LEGP collimator. All noise levels were calculated for $R_v=2.3$ kcps, based on the mean of the desired SU value range (2-2.5 kcps). R_p was set to range from the current average count rate $\bar{R}_{p,\text{SU}}$ to the desired value $R_p=3R_v=6.9$ kcps, using steps of 0.1 kcps per iteration. T_p ranged from 5-15 s and T_v from 10-30 s. For each iteration, $T_{\text{tot}}=T_v+T_p$ was increased by 1 s and optimal T_p/T_v -combination resulting in the lowest relative noise levels was saved. $A_{\text{perf}}=120$ MBq was assumed for $\bar{R}_{p,\text{SU}}$ and was scaled appropriately for higher R_p -values.

In order to see how different ventilation count rates and R_p/R_v -ratios may affect the quotient noise levels, both current and recommended modified parameter values were plotted for $R_v=0.5-4.0$ kcps and $R_p/R_v=1-5$ respectively.

4 Results

Validation of the MATLAB script resulted in good correlation with the results seen in the *Palmer et al. (2001)* study. As shown in *figure 3*, the same fractions of minimum at $T_p/T_v=0.5$ and $R_p/R_v=3$ was calculated when using the same criteria. In *figure 3*, MATLAB-simulated plots demonstrate how the relative standard deviation in quotient image Q varies with parameter ratios R_p/R_v and T_p/T_v whilst using the criteria that R_{tot} and T_{tot} are fixed, respectively. As seen in the figure, changing the ratio T_p/T_v can drastically change the resulting noise levels, whereas the noise levels barely change for $R_p/R_v > 1.5$. Therefore, knowledge regarding an optimal T_p/T_v ratio is important for eventual criteria and/or parameter combinations being used when performing V/P_{SPECT} studies.

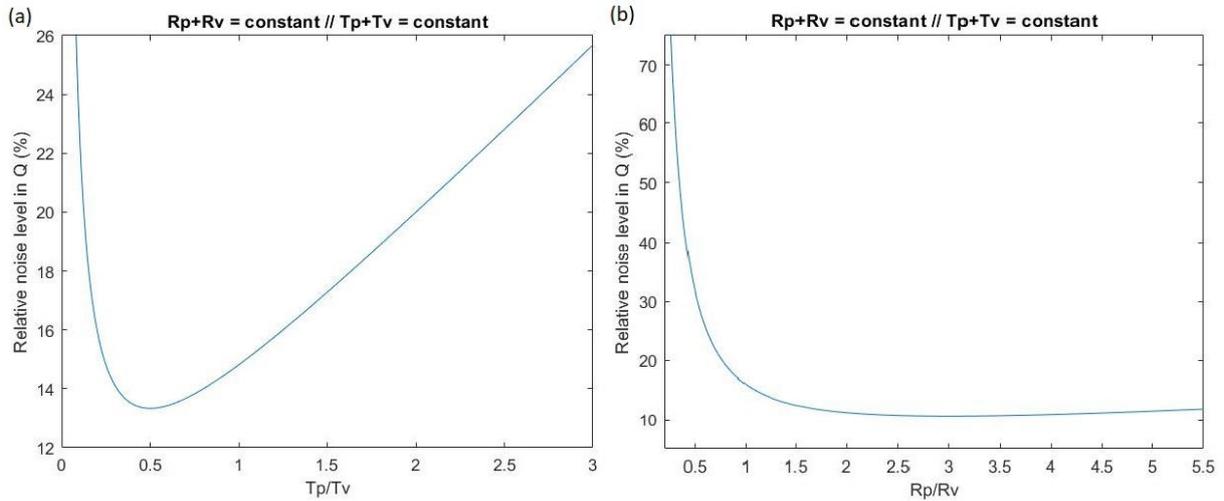


Figure 3: MATLAB simulation demonstrating how the relative noise level in quotient image Q changes with varied (a) T_p/T_v and (b) R_p/R_v fractions respectively. Both R_{tot} and T_{tot} are fixed values. Observe the minima located at $T_p/T_v = 0.5$ and $R_p/R_v = 3$, respectively

The detector sensitivity when using LEHR collimator in the phantom studies was estimated to ~ 40 cps/MBq, resulting in ~ 25 MBq being equivalent to the AP detector registering 1 kcps. *Figure 4* demonstrates reconstructed images for equivalent ventilation, perfusion-only and quotient for acquisition angle $1/120$ after using the *Arithmetic* tool in the *Xeleris* software. Parameter values for the starting angle in the AP-position were $R_v=4$ kcps ($A_{vent}=100$ MBq in phantom), $R_p=6$ kcps ($A_{perf}=150$ MBq in phantom), $T_p=5$ s and $T_v=10$ s, being displayed in a 64×64 matrix. The ROI being used for calculating relative standard deviation RSD is shown as a red rectangle in quotient image Q .

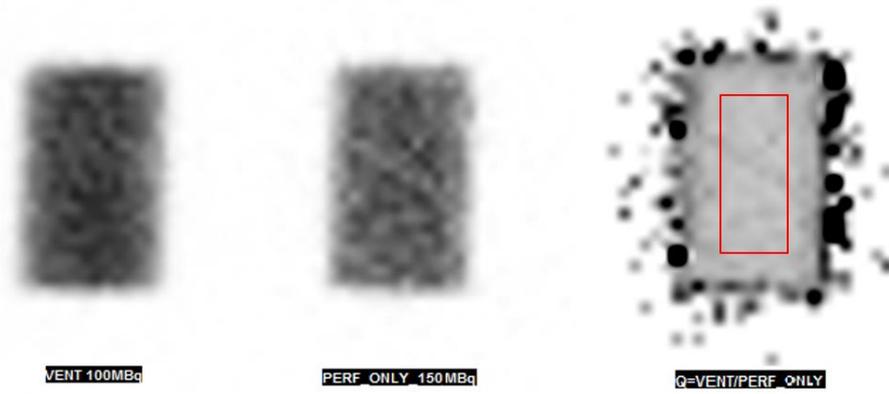


Figure 4: Reconstruction of quotient image Q, based on a phantom study with $R_v=4$ kcps, $R_p=9$ kcps, $T_v=10$ s and $T_p=5$ s. Images from the left: 1: ventilation image V, 2: perfusion-only image P, 3: quotient image Q. All pixel values in Q have been increased by a factor 10^3 . The ROI being used is shown as a red rectangle in Q. All images are based on acquisitions from angle $1/120$

The credibility of using the MATLAB script for estimating noise levels in quotient images is presented in *figures 5-7*. An overall resemblance in noise level variation can be seen when comparing the data points to each other. *Figure 5* demonstrates how the relative standard deviation varies in phantom study images and MATLAB simulations respectively, when the ventilation count rate R_v varied from 1-6 kcps (steps of 1 kcps) and other parameter values were fixed at $R_p=6$ kcps, $T_p=5$ s and $T_v=10$ s. Both plots follow the same descending/ascending trend and share a shallow minimum around $R_v=3.5$ kcps ($R_p/R_v=1.7$). Calculated noise levels follow the same pattern for $R_v=2-6$ kcps with the exception at $R_v < 2$ kcps where the noise levels in the phantom study increase faster at lower count rates compared to using the MATLAB script, possibly due to the solution not being properly mixed for the lower activity.

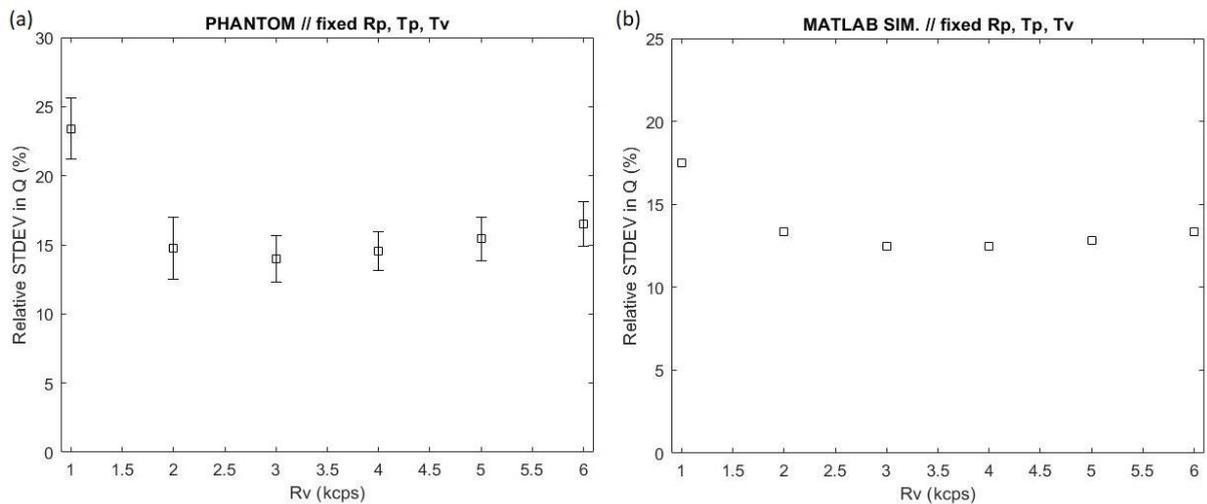


Figure 5: (a) Phantom study and (b) MATLAB simulations demonstrating the variation in relative standard deviation in quotient image Q (%) with $R_v=1-6$ kcps while other parameters values fixed at $R_p=6$ kcps, $T_p=5$ s and $T_v=10$ s. Error bars indicate sample standard deviation in relative noise levels based on 120 acquired images.

When the perfusion count rate R_p instead varied from 2-6 kcps (again with steps of 1 kcps), while other parameters are fixed at $R_v=2$ kcps, $T_p=5$ s and $T_v=10$ s the relative standard deviation in Q again follow the same pattern for both the phantom study and the MATLAB simulation (figure 6). Both plots show the same descending trend in noise levels as R_p becomes higher, stagnating for larger values.

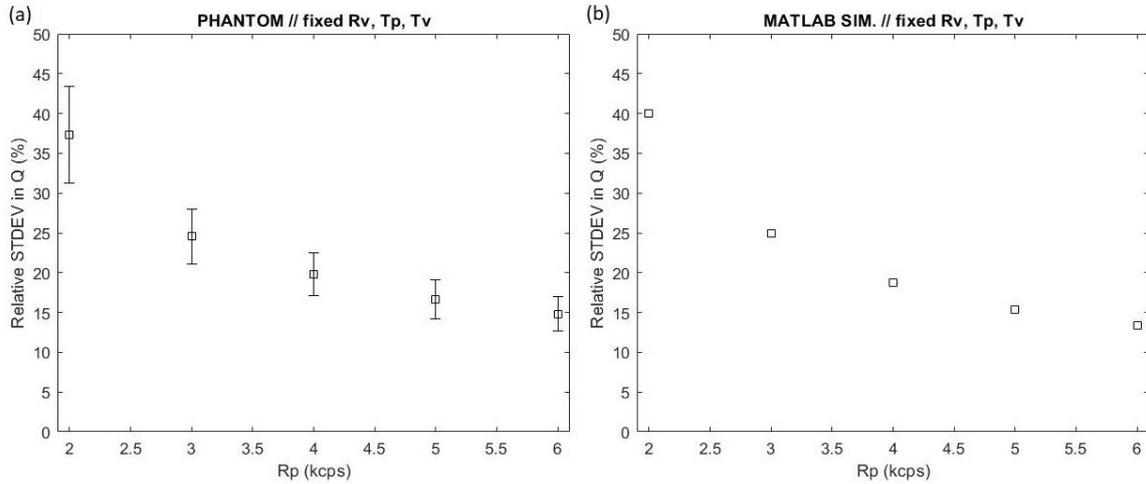


Figure 6: (a) Phantom study and (b) MATLAB simulations demonstrating the variation in relative standard deviation in quotient image Q (%) with $R_p=2-6$ kcps while other parameters values fixed at $R_v=2$ kcps, $T_p=5$ s and $T_v=10$ s. Error bars indicate sample standard deviation in relative noise levels based on 120 acquired images.

Figure 7 demonstrates how the relative standard deviation varies in phantom measurements and MATLAB simulations as ventilation acquisition time T_v varied from 1-10 s (steps of 1, 2, 5 and 10 s) respectively. Other parameters were fixed at $R_p=9$ kcps, $R_v=3$ kcps and $T_p=5$ s. Both plots show the same descending trend in noise levels as T_v becomes higher and slowly stagnating for larger values.

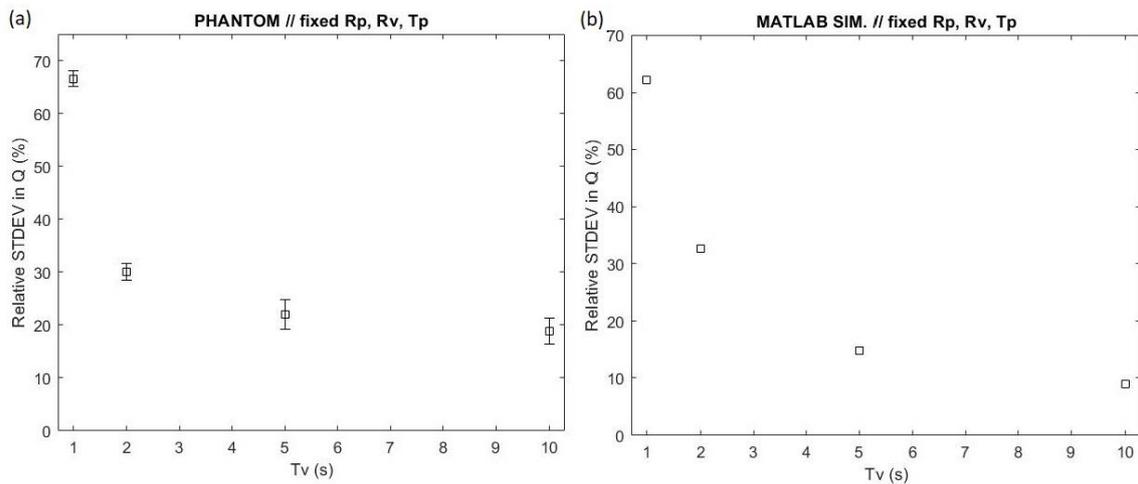


Figure 7: (a) Phantom study and (b) MATLAB simulations demonstrating how the relative standard deviation in quotient image Q (%) varies with $T_v=1-10$ s (1, 2, 5, and 10) and other parameters values fixed at $R_p=9$ kcps, $R_v=3$ kcps and $T_p=5$ s respectively. Error bars indicate a variance in noise levels based on 120 acquired images

Comparisons seen in *figures 5-7* indicate that calculations made using the MATLAB script were well correlated with the phantom study, implying that the script could be used in further evaluations of V/P_{SPECT} image quality with respect to relative noise levels. Based on the evaluation of the $n=37$ clinical V/P_{SPECT} studies at SU, the average perfusion and ventilation count rates equals $\bar{R}_{p,\text{SU}}=4.3\pm 0.8$ kcps and $\bar{R}_{v,\text{SU}}=2.3\pm 0.6$ kcps respectively.

To receive the recommended noise level in quotient images according to EANM guidelines different scenarios with values received using the LEHR collimator were calculated with the MATLAB script. A total of 8 optimized combinations were compiled (*table 5*), where combination 1 and 8 represented scenarios where either A_{perf} or T_{tot} had been modified. Remaining combinations represented scenarios where both parameters are modified, with combination 4 representing the middle ground. Total scan time and resulting effective dose $E=E_{\text{vent}}+E_{\text{perf}}$ is presented for each combination. E_{vent} is based on $A_{\text{vent}}=55$ MBq, which in turn is based on $\bar{R}_{v,\text{SU}}=2.3$ kcps. By only increasing the total scan time (combination 8), there is no need to increase the current administrated perfusion activity $A_{\text{perf}}=120$ MBq to the patient.

Table 5: Compilation of A_{perf} and T_{tot} combinations resulting in relative noise levels in quotient image Q within $\pm 1\%$ of acquired noise levels as when using recommended EANM guidelines. Combination 1 and 8 represents situations where only A_{perf} and T_{tot} have been increased respectively. Combination 2-7 represent situations where A_{perf} and T_{tot} are both increased. Optimal acquisition time distribution and total scan time is presented for each combination

Combination #	A_{perf} [MBq]	R_p [kcps]	T_{tot} [s]	T_v [s]	T_p [s]	Total scan time [min]	E [mSv]
1	193	6.9	15	10	5	21	2.9
2	176	6.3	16	11	5	22	2.8
3	165	5.9	17	11	6	23	2.6
4	153	5.5	18	12	6	24	2.5
5	142	5.1	19	12	7	25	2.4
6	137	4.9	20	13	7	26	2.3
7	128	4.6	21	13	8	27	2.2
8	120	4.3	22	14	8	28	2.1

Figures 10 and 11 demonstrate the change in relative standard deviation in quotient image Q as R_v and count ratio R_p/R_v varies from 0.5-4.0 kcps and 1-5, respectively. Parameter combinations 1, 4 and 8 from *table 5* (red, yellow and purple, respectively) are plotted with a fourth plot (blue) representing current parameters values used at SU as reference. Noise levels are more/less affected as R_v changes depending on the used R_p -value (see *figure 10*). Only increasing the total scan time results in the least affected noise levels for normally received R_v -values at SU ($R_{v,\text{SU}}=1.8-2.9$ kcps, based on the $n=37$ clinical studies). An exponential increase in noise levels can be seen for all plots around $R_v=1.5$ kcps. Depending on the T_p/T_v ratio, the local R_p/R_v minimum is located around 1.7-1.8 (*figure 11*). A high variance in R_p/R_v ratios have little to no effect on the resulting noise levels with the exceptions of being very high.

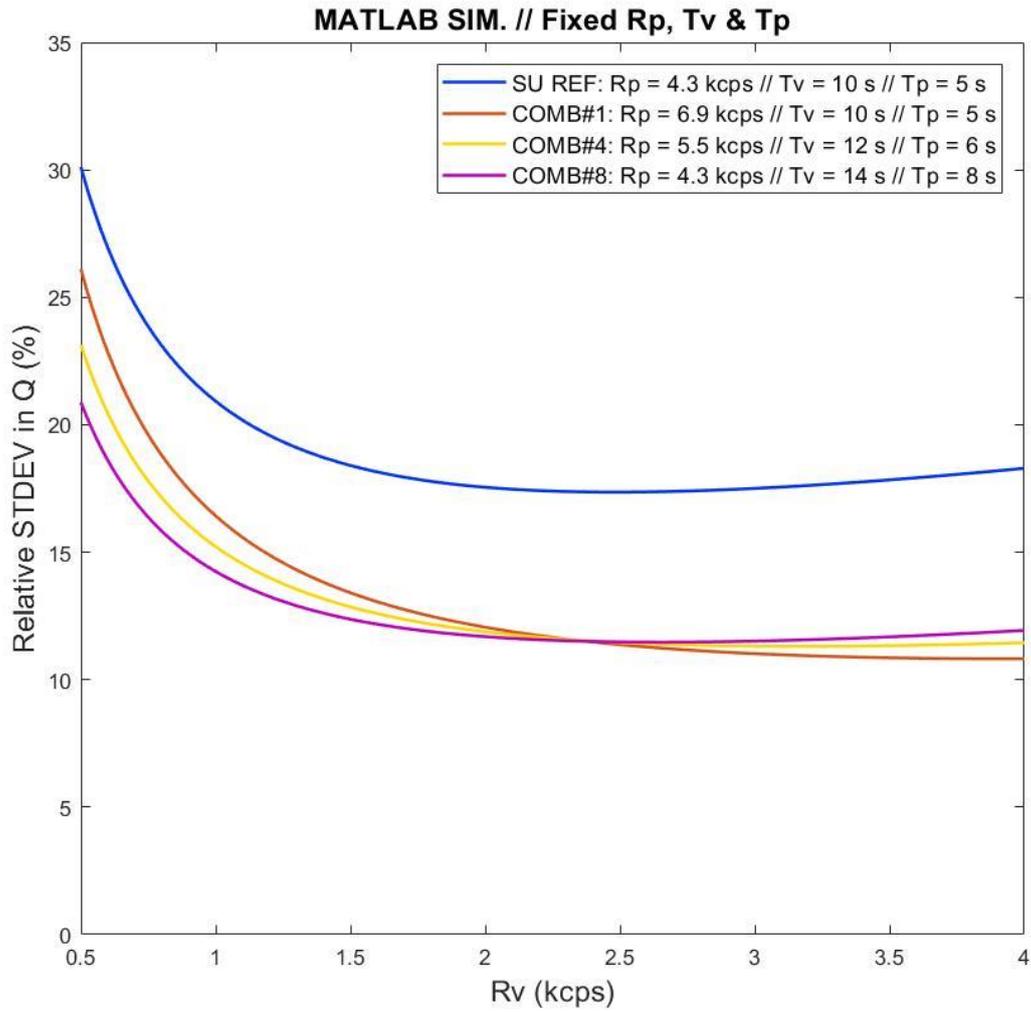


Figure 10: Demonstrating how the relative standard deviation in Q is affected when acquiring different ventilation count rates whilst using different parameter combinations. Three parameter combinations (1,4 and 8) from table 5 are plotted for $R_v=0.5-4.0$ kcps with a fourth plot using the current SU parameter values for R_p , T_p and T_v as reference

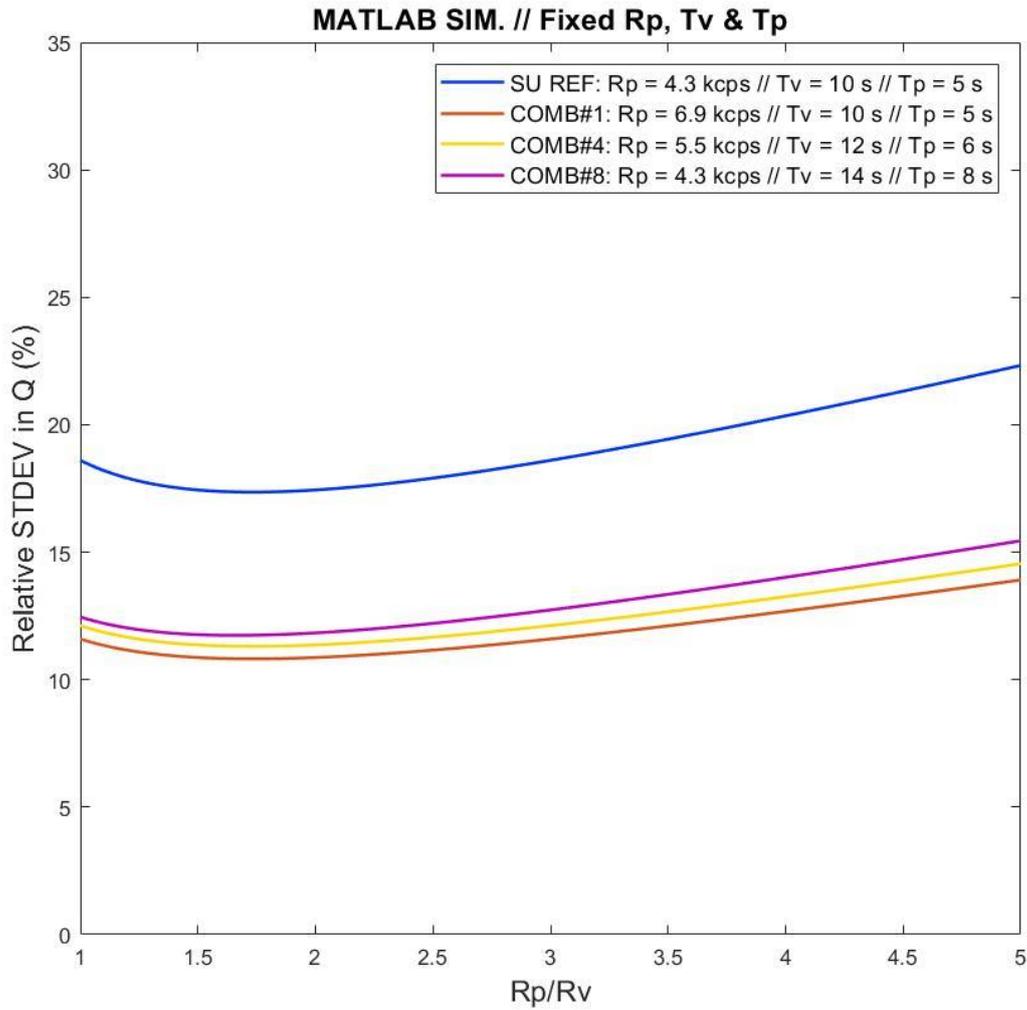


Figure 11: Demonstrating how the noise level in Q is affected when acquiring different R_p/R_v ratios whilst using different parameter combinations. Parameter combinations (1,4 and 8) from table 5 are plotted for $R_p/R_v = 1-6$ kcps with a fourth plot using the SU parameter values for R_p , T_p and T_v as reference. Depending on the T_p/T_v ratio being used, the local R_p/R_v minimum varies from 1.7-1.8

5 Discussion

Since there is a high tolerance in varying R_v and the resulting R_p/R_v ratio without truly affecting the quotient image quality, current $\bar{R}_{v,SU}$ variance has little to no impact on the resulting noise levels (*figure 10*). The real issue is the high R_p -fluctuation with a current perfusion count rate variance of $\pm 20\%$ based on the $n=37$ clinical studies at SU. Having such a large variance in count rate is troubling as R_p has a big impact on the resulting noise levels in the quotient image (*figure 9*). There may be several patient-related factors resulting in varying pulmonary uptake of MAA, along with difference in radiochemical purity. Clearance is not considered a crucial factor as the biological half-life of ^{99m}Tc -MAA is 2-3 hours and the perfusion tomography is performed directly after administration [1].

One known issue that contributes to the R_p -fluctuation is that not all the perfusion activity is administrated to the patient due to a varying amount still being in the syringe after the administration. It is therefore important that all personnel performing V/P_{SPECT} studies make sure that the patient receives the prescribed activity. Measuring the remaining activity in the used syringe for each examination, the average remaining activity can be used to adjust the current administration. One solution in achieving less R_p -variance is to tailor the administrated perfusion activity to each patient. One such administration method is presented in *Gales et al. (2015)*, where it is suggested that the count rate on the camera should indicate which A_{perf} is to be used. The administration of ^{99m}Tc -MAA would therefore stop when the desired count rate is acquired, minimizing R_p -variance and tailoring the patient's perfusion dose [16]. Today no reference dosage is present specifically for V/P_{SPECT} studies (only for V/P_{PLANAR}) which indicates that an optimal activity amount during perfusion SPECT-imaging needs to be further investigated and validated. However, the resulting patient dose should always be as low as reasonably possible and the combination of choice should be made based on the state of each patient.

The equation used in the MATLAB script was applied from the study by *Palmer et al. (2001)* to compile the current recommended count rate and acquisition time ratios. This equation has been proven to be a viable method to evaluate image quality regarding noise levels in the quotient images [2]. In the study, criteria were used where the sum of both the ventilation and perfusion count rate $R_{tot}=R_p+R_v$ and ventilation and perfusion acquisition time $T_{tot}=T_p+T_v$ were considered fixed values [2]. The choice of using the criteria is not clarified in the study. When removing these criteria, allowing all parameters to be changed freely, optimal count ratios changes drastically, both seen in the phantom study (*figure 5a*) and when using the validated MATLAB script. When inserting the optimal T_p/T_v combinations presented in *table 5* (where optimal T_p/T_v range from approximately 0.5-0.6), optimal R_p/R_v ratios varied from 1.7-1.8 depending on the T_p/T_v of choice, being a significant change compared to the current recommended count ratio $R_p/R_v=3$. When implementing the current recommended time ratio $T_p/T_v=0.5$, the optimal count ratio equals $R_p/R_v=1.7$. Despite these differences, in the end, acquiring varying R_p/R_v ratios have little impact on the resulting quotient image quality (*figure 11*).

Validation of the credibility of the MATLAB script was expected as noise levels in scintigraphy images are generally considered non-correlated [2]. This fact can be further strengthened as the parameters and ratios used today are mainly based on the same mathematical evaluation as being used in the MATLAB-script [2].

According to EANM guidelines, it is recommended to use a LEGP collimator when performing V/P_{SPECT} . Compared to the LEHR collimator used at SU a LEGP collimator requires only ~50% of the administered activity to achieve the same count rate [1-2]. The downfall using a LEGP collimator is a reduction in image resolution that may reduce the chances of detecting PE in smaller segments. Despite this it is still the recommended choice as the authors deemed it to be sufficient [2]. V/P_{SPECT} studies are performed using a LEHR collimator at SU and demands that the patient is ventilated with a higher activity amount (compared to if a LEGP collimator is used), when trying to achieve the desired ventilation count rate $R_v=2-2.5$ kcps. This fact can be strengthened further when reviewing the detector sensitivity that was tested during the phantom studies, where ~25 MBq was needed in order to acquire 1 kcps, indicating that around 50-60 MBq is needed to acquire the desired ventilation count rate at SU – twice of what is recommended by EANM [1-2,5].

Using a LEHR collimator also drastically reduces the perfusion count rate acquired at SU as no parameter modifications have been made, e.g. neither with a higher $^{99\text{m}}\text{Tc}$ -MAA activity amount nor longer scan times [2,5]. This reduction in perfusion count rate can be confirmed through the evaluation of the $n = 37$ SU parameter values, where the average perfusion count rate $\bar{R}_{p,\text{SU}} = 4.3 \pm 0.8$ kcps is ~62% of what is achieved through using EANM guideline-based values [1-2,5]. It is therefore recommended to use any of the modified parameters combinations presented in *table 5*, ensuring the same noise levels as when using the EANM recommended LEGP collimator.

Regarding the compiled parameter combinations, only increasing the total scan time from 21 to 28 minutes (combination 8, *table 5*) will result in noise levels being the least affected in the region of lower R_v -values compared to other parameter combinations (*figure 10*). With the average acquired ventilation count rate at SU being $\bar{R}_{v,\text{SU}} = 2.3 \pm 0.6$ kcps, the tolerance for R_v is high when using this combination. No additional radiation dose would be added to the patient ($E=2.1$ mSv) and the clinical impact due to the increased scan time should be minimal. For patients that are comfortable with the increased scan time, this combination is the preferred choice.

If, however, the patient is unable to comfortably stay still during the extended scan time from 21 to 28 min, either combination 1 or 4 from *table 5* is recommended. If possible, combination 4 is the preferred choice due to noise levels being less affected for lower R_v -values, along with a lower effective dose compared to using combination 1. A_{perf} would be increased from 120 to 153 MBq ($E=2.5$ mSv), a 40 MBq difference compared to only increasing the administered perfusion dose in combination 1. Using combination 4, the total scan time is only increased by 3 minutes (from 21 to 24 min), and should in many cases be possible for the patient to stay comfortably still during each tomography. A similar combination is used at the Karolinska University Hospital (KU), Huddinge, where a LEHR collimator is used along with $A_{\text{vent}}=50$ MBq, $A_{\text{perf}}=150$ MBq, $T_v=16$ s and $T_p=8$ s [15]. This combination results in lower noise levels than what is achieved using EANM-recommended values.

In worst case scenarios combination 1 can be used, keeping the current total scan time of 21 minutes. Using combination 1, administered perfusion activity would be increased from 120 to 193 MBq ($E=2.9$ mSv). In scenarios like this, where no other options are available, the increased perfusion dose to save time is considered justified as it may increase the chances of correct diagnosis [4].

As the LEHR collimator is used at SU, it is recommended to change the current display resolution from 64×64 to 128×128 . This would increase the image quality to its fullest potential. Higher resolution combined with lower noise levels could potentially increase the chances of detecting smaller mismatched areas in the quotient image [1-2,4]. The resolution can always be lowered if needed and the computational storage space required for images using higher resolution should not be a problem as the frequency of V/P_{SPECT} studies at SU is fairly low.

Regarding the phantom studies, the dedicated gamma camera scan table adds additional noise in quotient images due to attenuation in the material. It may also create correlative noise distribution in some of the resulting images, for example in images where only a portion of the phantom is covered by the scan table. Having the phantom mounted on a contraption allowing it to hang freely would be a more ideal situation. Doing this would lower the RDS variance and ensure that the noise distribution is non-correlative for all angles.

6 Conclusion

V/P_{SPECT} is considered one of today's most reliable imaging techniques for accurately diagnosing PE. When performing V/P_{SPECT} , a 3 to 1 perfusion to ventilation count rate is currently recommended by EANM to achieve the lowest relative noise levels. Due to the varying physical state of patients, there is a high variation in acquired ventilation count rates, often leading to non-optimal count ratios. A MATLAB script was developed to study how varying ventilation count rates and count ratios affect quotation image quality, focusing on relative noise levels. The same script was further used to compile modified parameter combinations at SU to compensate higher relative noise levels due to using a LEHR collimator instead of the EANM recommended LEGP collimator.

The results indicate that the impact on image quality when acquiring varying count ratios is low when performing V/P_{SPECT} . Instead image quality depends highly on the obtained perfusion count rate and acquisition time distribution. SU is recommended to change their current administered perfusion dose and/or acquisition time to compensate for using a LEHR collimator.

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Appendix

1. MATLAB script compilation

An .m-file was created containing the relative noise function that could be used in the main script for the noise level calculations. The MATLAB function tool was used to create the function $\text{Noise} = f(T_p, T_v, R_p, R_v) = \text{Eq. 2}$. After the function script had been created, the main noise calculation script was formed. In this script, four for-loops was created. - one for each parameter in the Noise-equation. Within the last for-loop, an if-loop was added in which eventual criteria can be inserted by the user.

In the for-loop for each variable, either a fixed value or an interval can be inserted. In an interval is inserted, for example $1 < T_p < 10$ s, each value will be used in the noise level function and stored if eventual criteria are met. All accepted calculations are stored in a dedicated column in a matrix M. For each stored calculation, the value of each parameter used in that calculation is stored in the same matrix in a dedicated column. For example, the first four columns in the matrix M contains the values for T_p , T_v , R_p and R_v . Other columns in the same matrix contains other values based on variables, such as ratios R_p/R_v and T_p/T_v or calculations such as difference between calculated noise value and noise value based on guideline values (%). Before the loop section, vectors are created for each variable (for example VectorTp containing all T_p -values used in an interval) and other calculated values and ratios. These vectors are proactively filled with calculated values from each iteration that has passed eventual criteria and has been stored in the respective column of the matrix M.

```
function Noise = f(Tp, Tv, Rp, Rv)

%Relativt brus i kvotbild Q = V/P (%)

Noise = (((Rp + Rv) * Tp)^2 / (Rv * Tv)) + (Rp + Rv) * Tp / (((Rp + Rv) * Tp -
(Tp / Tv) * Rv * Tv)^2);

end

-----

clc
format short

a = 0;
x = 1;
M = zeros(x, 9);
%Skapa vektorer
VectorRv = zeros(x, 1)';
VectorRp = zeros(x, 1)';
```

```

VectorRptotRv = zeros(x,1)';
VectorRpRv = zeros(x,1)';
VectorQ = zeros(x,1)';
VectorTp = zeros(x,1)';
VectorTv = zeros(x,1)';
VectorTpTv = zeros(x,1)';
VectorNoise = zeros(x,1)';

for Tp = 10      %Insamlingstid/vinkel perfusion (s)
    for Tv = 16      %Insamlingstid/vinkel ventilation (s)
        for Rp = 250      %Count rate bidrag från perf (kcps)
            Rp = Rp/100; %Upplösning Rp
                for Rv = 50:2000 %Count rate bidrag fråmn vent (kcps)
                    Rv = Rv/100; %Ändra upplösning för Rv

                    Noise = f(Tp,Tv,Rp,Rv); %Relativ brusnivå i Q

                    if Tp < 1 %Utvalda kriterier för aktuell simulering.
                        a;
                    %elseif Tp+Tv > 19
                        a;
                    %elseif Tp+Tv < 19
                        a;
                    %elseif (Tv+Tp)/15 > 1.50
                        a;
                    %elseif Rp/3.6 > 1.50
                        a;
                    %elseif Noise/f(5,10,6.75,2.25) < 0.99
                        a;
                    %elseif Noise/f(5,10,6.75,2.25) > 1.01
                        a;

                    else
                        a = a + 1;

                    %Placering av parametrar/uträkningar i matris M

                    M(a,1) = Tp;      %Tp (s)
                    M(a,2) = Tv;      %Tv (s)
                    M(a,3) = Rp;      %Rp (kcps)
                    M(a,4) = Tp+Tv; %Ttot (s)
                    M(a,5) = ((Rp/3.6)*100)-100;% Ökning Rp (%)
                    M(a,6) = (((Tv+Tp)/15)*100)-100; %Ökning Ttot(%)
                    M(a,7) = Tp/Tv; %Tp/Tv-kvot
                    M(a,8) = Rp/Rv; %Rp/Rv-kvot
                    M(a,9) = (Noise/f(5,10,6.75,2.25))*100;

```

```

%Brusnivå gentemot värden från guidelines (%)

VectorRv(a) = Rv; %Fylla vektorer.
VectorRp(a) = Rp;
VectorRpRv(a) = Rp/Rv;
VectorRptotRv(a) = (Rp+Rv)/Rv;
VectorQ(a) = M(a,8);
VectorTv(a) = M(a,2);
VectorTp(a) = M(a,1);
VectorTpTv(a) = M(a,1)/M(a,2);
VectorNoise(a) = Noise*100;

end
end
end
end
end

M;

Noise_VS_Guidelines = round(min(M(:,9)),2);
%Brusnivå vs guidelines (%)

plot(VectorRpRv,VectorNoise)
%Plottar utvalda vektorer mot varandra

axis([0.5 5 0 40])

hold on

```