Factors Affecting Standardized Uptake Value (SUV) of Positron Emission Tomography (PET) Imaging with ^{18}F-FDG

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Objective: *The purpose of the study was to study factors affecting SUV of PET imaging with ^{18}F-FDG.*
Material and Method: *PET/CT Biograph 64 was used to acquire the data. A NEMA PET phantom with 6 spheres varying in diameter from 10 to 37 mm was used to mimic the human body and tumors. Background activity of ^{18}F in the phantom was 0.14 µCi/ml and tumor-to-background ratios (TBR) of 2:1, 5:1 and 10:1 were studied. For each TBR, thirty sinograms were acquired with 3-min scan durations. Different scan durations varying from 3 to 20 min using a TBR of 5:1were studied and three datasets of each scan time were collected. Sinograms were reconstructed using the Ordered Subset Expectation Maximization (OSEM) algorithm with 5 mm Full-Width-at-Half-Maximum (FWHM) Gaussian filtering. Sinograms at TBR of 5:1 were reconstructed by varying the number of iterative updates of OSEM (N) from 8 to 168 and SUV_{avg} and SUV_{max} were measured. The percentage of underestimation of SUVs was used to study the effect of tumor size and TBR. Intraclass correlation coefficient (ICC) was used to test the reliability of SUV_{max} with different scan durations.*
Results: *The results showed that both the SUV_{avg} and SUV_{max} rapidly increased when N was < 48 and slightly increased afterwards. At TBRs ranging from 2:1 to 10:1, the percentages of underestimation of SUV_{max} ranged from 8.17 to 22.46 and that of SUV_{avg} were ranged from 41.44 to 52.33 for 37-mm sphere and from 40.38 to 54.52 and from 48.97 to 67.73 for 10-mm sphere respectively. Different scan durations gave reliable $SUVs_{max}$ with ICC of 0.996.*
Conclusion: *SUVs increased as N increased. The percentage of underestimation of the SUV depended on tumor size and TBR. Scan duration did not affect SUVs.*

Keywords: *Standardized uptake value (SUV), Positron emission tomography (PET), Factors affecting, ^{18}F-FDG*

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Positron Emission Tomography (PET) has been increasingly used as a tool for tumor diagnosis, staging and differentiating malignant tumors from benign tumors and for assessing treatment efficacy in patients with various cancers. PET imaging is based on radiotracer compounds labeled with positron-emitting radionuclides and injected into the subject of the present study. This radiopharmaceutical can then be used to track biochemical and physiological processes *in vivo*. The largest area of clinical use of PET is in oncology and 2-[fluorine-18] fluoro-2-deoxy-D-glucose (^{18}F-FDG), glucose analog, is the most widely used radiopharmaceutical because of their increased glucose metabolism in tumor cells. Although qualitative interpretation is mainly used, quantitative indices are used to assess tumors and to follow-up their responses to therapy. Standardized uptake value (SUV) is a quantitative measurement of radioactivity concentrations at a fixed time and it increases continuously in tumor cells as a function of time after

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^{18}F-FDG intravenous administration. The SUV has been defined as tissue concentration (kBq/ml) divided by activity injected per body weight (kBq/g)(1-4).

Despite the popularity of SUV, the reliability of SUV is still somewhat debating. The primary problem with the SUV is that it is subjective to too many sources of variability which are not controlled such as glucose level, length of the uptake period, body weight, body composition, recovery coefficient and partial volume effect (PVE)(5). Ivanovic et al(6) showed the large variations in the calculated SUVs as a function of selected imaging protocols with different acquisition and image reconstruction parameters. Feuardent et al(7) reported that differences in SUVs greater than 100% could be caused by only differences in the data acquisition and processing. Biases in SUVs only slightly depend on the emission scan duration and on the presence of out-of-the-field-of-view activity, but strongly depend on the attenuation coefficient (μ) map used for attenuation correction. Moreover, they found that the smaller the sphere, the greater the SUV underestimation. Some literature(3,6,8) found that an increasing number of iterative updates in ordered subset expectation maximization (OSEM) reconstruction also resulted in increasing in SUVs.

Due to the inconstancy of SUV misleading the clinician's interpretation, factors affecting SUV are of interest. The present research was aimed to study factors affecting SUV of PET imaging with ^{18}F-FDG such as number of iterative updates (number of iterations x number of subsets), tumor size, tumor-to-background activity ratio (TBR) and emission scan duration (preset time). Phantoms were assigned to mimic the human body and tumors.

Material and Method

Phantom studies

The NEMA PET body phantom with the size of 23 x 30 cm and 17.7 cm high as shown in Fig. 1A was used. The asymmetric shape with a total volume of ~9,986 ml of this phantom was an approximate simulation of the human body in the part of thorax or abdomen. Six spheres (37 mm, 28 mm, 22 mm, 17 mm, 13 mm and 10 mm in diameter) inside the phantom as shown in Fig. 1B and 1C were used to mimic tumors.

In the present study, ^{18}F was used instead of ^{18}F-FDG and the concentration of the background activity in the NEMA PET body phantom was 0.14 μCi/ml which was used in a routine whole body scan(9). From the pilot study in 50 patients at Bumrungrad International Hospital, the result showed that TBRs were ranging from 2:1 to 21:1 and three TBRs of 2:1, 5:1 and 10:1 were selected due to high frequencies.

The Ge-68 and NEMA PET scatter phantoms were used to simulate radioactivity from the outside of the field of view (FOV). Ge-68 phantom was used to mimic scatters from a patient's head and NEMA PET scatter phantom was used to generate scatter from the lower part of the body. Fig. 2 shows the position of three phantoms used in the present research.

Data acquisition and image processing

NEMA PET body Phantom was imaged by PET/CT Siemens Biograph 64 TruePoint system with 3D acquisition mode. Firstly, CT scan was performed with matrix size of 256 x 256 and 3-mm slice thickness and then PET data was sequentially acquired with 3-min scan duration. After random coincidence subtraction and correction for scatter and attenuation (CT-base attenuation map), the data were rebinned into 2D sinograms using Fourier rebinning. The transverse images were reconstructed onto a 168 x 168 matrix size using OSEM algorithm with 5-mm Gaussian filter. The image protocol as described above was used throughout the entire research.

Number of iterative updates and determination the optimal number

The TBR of 5:1 was used in the present study because it was the one of the highest frequency of

Fig. 1 (A) NEMA PET body phantom, (B) the circular cover with six spheres attached and (C) a cross section of the NEMA PET body phantom with six spheres

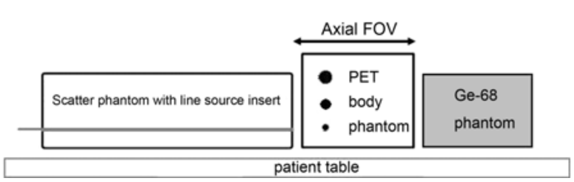

Fig. 2 The positions of three phantoms; NEMA PET body phantom was sandwiched between Ge-68 and scatter phantoms

TBR observed in 50 patients. The effects of number of iterative updates (number of iterations x number of subsets) on SUV were studied by varying number of iterative updates from 8 to 168.

Mean SUV_{avg} and mean SUV_{max} of all sphere sizes obtained from a different number of iterative updates of thirty datasets were computed. To determine the optimal number of iterative updates, the number that gave SUV close to the true SUV and compromising between image resolution and noise would be selected and applied for the rest of the present study.

Tumor (sphere) size

Thirty sinograms of the NEMA PET body phantom at TBR of 5:1 from the previous session were used in the present study. Mean SUV_{avg} and mean SUV_{max} of all sphere sizes of thirty datasets were computed. For each sphere size, the percentages of underestimation of SUV_{avg} and SUV_{max} were calculated as mathematically described in equation 1 and then compared.

$$\% \text{ underestim action} = \frac{\text{true SUV-measured SUV}}{\text{true SUV}} \text{ x } 100$$

Tumor-to-background activity ratio (TBR)

Three TBRs of 2:1, 5:1 and 10:1 were used. For Each TBR thirty acquisitions of NEMA PET body phantom and spheres were performed using the same imaging protocols. Then mean SUV_{avg} and mean SUV_{max} of all sphere sizes of thirty datasets were computed. For each TBR and sphere size, the percentages of underestimation of SUV_{avg} and SUV_{max} were determined.

Emission scan duration (preset time)

Sinograms of NEMA PET body phantom with TBR of 5:1 were acquired for five different preset times such as 3, 5, 10, 15 and 20 minutes, respectively and sequentially. Three datasets of each scan duration were taken. Mean SUV_{max} obtained from different emission scan durations for all data were determined. Intraclass Correlation Coefficient (ICC)(10) was used to determine the reliability or the agreement among values of SUV_{max} obtained from five different emission scan durations. The model of ICC was two-way random since there were two factors affecting the SUV_{max} *i.e.* emission scan duration and sphere size. If ICC approached to 1 that meant there was no variation within SUV obtained from different emission scan duration.

SUV measurement

Circular volumes of interest (VOIs) were manually drawn from CT images, placed in the center of each sphere and fitted with the inner-border of the sphere. After mapping VOIs on PET data, SUV_{avg} and SUV_{max} were automatically determined. True SUV was able to be determined because of knowing the activity and total weight of the phantom as described in equation 2 (7):

$$\text{True SUV} = \frac{\text{activity concentration in VOI (kBq/mL)}}{\text{injected activity (kBq)/total weight (g)}}$$

In the present research, true SUVs of six spheres were 2.6 for TBR of 2:1, 6.51 for TBR of 5:1 and 13.2 for TBR of 10:1.

Results

Number of iterative updates and determination of the optimal number

Fig. 3 demonstrates the image quality of reconstructed images as a function of number of updates. The results showed that for all sphere sizes, the mean SUV_{avg} increased when increasing number of updates from 8 to 48. The mean SUV_{avg} was slightly increased when the number of updates increased from 56 to 168. Similarly the mean SUV_{max} was increasing as the number of updates increased and it slightly increased when the number of updates was more than 48. When SUVs were plotted as shown in Fig. 4A and 4B, they demonstrated that for both mean SUV_{avg} and mean SUV_{max} the graphs had the plateau when the number of updates was more than 48. The number of updates of 64 was used as the optimal number and applied for the rest of the present study because it gave the trade-off between image noise and resolution for all sphere sizes.

Tumor (sphere) size and TBR

There were six sphere sizes of 37 mm, 28 mm, 22 mm, 17 mm, 13mm and 10 mm at three different TBRs of 2:1, 5:1 and 10:1 used in this study. At TBR of 2:1, the percentages of underestimation of SUV_{avg} and SUV_{max} of six spheres were 41.44% and 8.17%, 44.13% and 12.94%, 45.24% and 21.55%, 45.37% and 22.41%, 48.93% and 34.30%, and 48.97% and 40.38% respectively, at TBR of 5:1 were 46.58% and 20.68%, 54.02% and 25.97%, 56.56% and 31.17%, 57.84% and 35.46%, 61.46% and 44.21%, and 65.93% and 55.56% respectively and at TBR of 10:1 were 52.33% and 22.46%, 55.83% and 30.04%, 56.59% and 33.32%, 62.29% and 39.87%, 62.63% and 54.37%, and 67.73% and 54.52% respectively. The

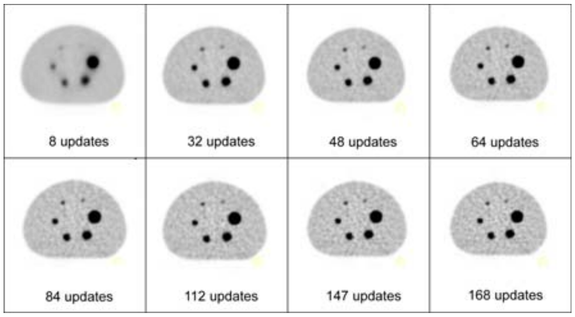

Fig. 3 Reconstructed PET images using different number of iterative updates. More number of iterative updates introduced more noise in the images

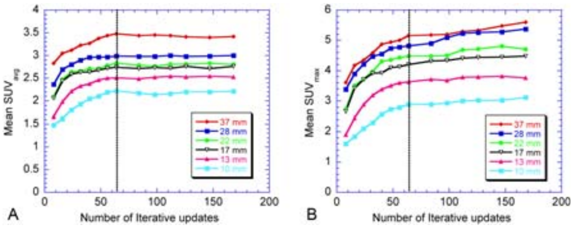

Fig. 4 (A) Mean SUV_{avg} as a function of number of iterative updates for the sphere size of 37 mm, 28 mm, 22 mm, 17 mm, 13mm and 10 mm and (B) mean SUV_{max} as a function of number of iterative updates for the sphere size of 37 mm, 28 mm, 22 mm, 17 mm, 13mm and 10 mm

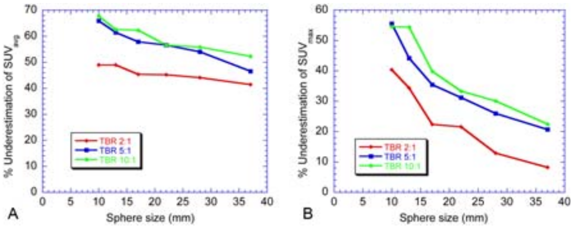

Fig. 5 (A) The percentages of underestimation of SUV_{avg} as a function of sphere size for TBR of 2:1, 5:1 and 10:1 and (B) the percentages of underestimation of SUV_{max} as a function of sphere size for TBR of 2:1, 5:1 and 10:1

percentages of underestimation of SUV_{avg} and SUV_{max} increased when sphere size decreased as shown in Fig. 5A and 5B respectively. The percentages of underestimation of SUV_{avg} and SUV_{max} trended to increase as the TBR increased. Fig. 6 shows the partial volume effect which were probably leading to underestimation of SUV in PET images.

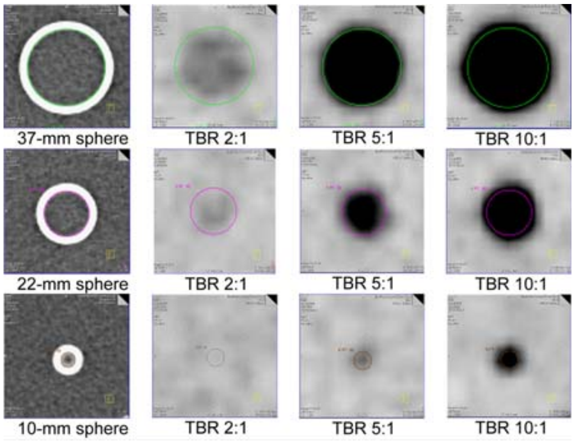

Fig. 6 The examples of partial volume effect (PVE) in PET images of 37 mm, 22 mm and 10mm sphere size (upper, middle and lower row respectively) with the TBR of 2:1, 5:1 and 10:1 (second, third and fourth column respectively). First column showed the CT images of each sphere size

Emission scan duration

The results showed that for the sphere size of 37 mm, the mean SUV_{max} were 4.93, 4.85, 4.89, 4.99 and 4.88 at 3 min, 5 min, 10 min, 15 min and 20 min respectively. The mean SUV_{max} of the sphere size of 28 mm were 4.79, 4.61, 4.47, 4.66 and 4.44, for the sphere size of 22 mm were 4.73, 4.83, 4.48, 4.46 and 4.48, for the sphere size of 17 mm were 4.17, 4.08, 4.09, 3.87 and 3.8, for the sphere size of 13 mm were 3.56, 3.42, 3.35, 3.38 and 3.36, for the sphere size of 10 mm were 2.63, 2.74, 2.88, 2.74 and 2.81 at scan duration of 3 min, 5 min, 10 min, 15 min and 20 min respectively. From the test of the agreement of the mean SUV_{max} with different scan durations, the result showed that the ICC was 0.996 and 95% confidence interval ranging from 0.987 to 0.999. That meant the SUV_{max} at different scan durations was reliable or there was no statistically significant difference in SUV_{max}. The plot of mean SUV_{max} as a function of emission scan duration for all sphere sizes seemed to be constant as shown in Fig. 7. Moreover, the result showed that the image quality of PET images improved when the emission scan duration increased

Discussion

Using OSEM reconstruction algorithm, both SUV_{avg} and SUV_{max} increased rapidly when the number of iterative updates was less than 48 but slightly increased from 56 to 168. When plotting the graph

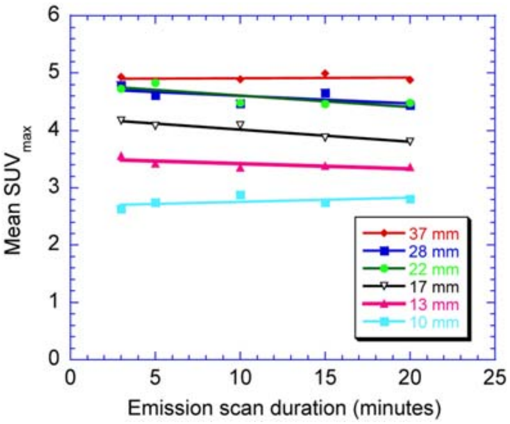

Fig. 7 Mean SUV$_{max}$ as a function of emission scan duration for all sphere sizes

between SUV and number of iterative updates, it showed the plateau when number of iterative updates was more than 48. According to the properties of OSEM algorithm, when increasing number of updates the image resolution improved but image noise increased. These results were a little bit different from that of Jaskowiak at el(3). They found that the SUV$_{avg}$ trended to rapidly increase with a number of iterations less than 5 iterations or 140 updates and slightly increased afterward. Whereas, SUV$_{max}$ continuously increased as the number of iterations increased. Ivanovic M et al(11) also reported that SUV$_{max}$ were changing from 6% to 70% when the number of iterations varied from 2 to 10 (16 to 80 updates) and SUV$_{max}$ also increased as a number of iterative increased. The authors concluded that in PET imaging number of iterative updates affected both SUV$_{avg}$ and SUV$_{max}$. Therefore, in a follow-up study, it should be aware of the image protocols that need to be similar to the previous protocols.

From the present research, measured SUVs of all sphere sizes were underestimated. Both the percentages of underestimation of SUV$_{avg}$ and SUV$_{max}$ increased in smaller sphere than larger sphere and trended to increase with increasing TBR. These results agreed with Feuardent et al(7). They found that the smaller sphere the higher SUV underestimation (35% and 91% for the 33-mm and the 10.5-mm sphere respectively). Soret et al(12) also studied the effect of tumor diameter on TBR and SUV. Their results showed that SUV was underestimated up to 85% for a 5-mm tumor. These results demonstrated that partial volume effect (PVE) made the bias SUV depending on tumor size. The nonlinear correlation between SUV and tumor size caused by PVE has been shown in several clinical studies. Vesselle et al(13) and Hallett et al(14) reported that small tumors appeared to be less aggressive than they actually were. This dependence was extremely confounding in the context of therapeutic follow-up. Indeed, if a tumor shrunk in size as the course of therapy progressed, then it would erroneously appear to have less activity when it was small. Even if the true metabolic rate has stayed constant or increased slightly, PVE might cause an erroneous decrease in apparent uptake(15).

The results from the present research showed that SUV$_{avg}$ were more underestimated than SUV$_{max}$. SUVs were strongly underestimated to 55% and 70% for SUV$_{max}$ and SUV$_{avg}$ respectively in 10-mm tumor at TBR of 10:1 but only 8% and 40% for SUV$_{max}$ and SUV$_{avg}$ respectively in 37-mm tumor at TBR of 2:1. For this effect, partial volume effect may play an important part in underestimation of SUV. Biases in SUV strongly depend on tumor size and this dependence is extremely confounding in the follow-up study. If the tumor shrinks slightly in size during the therapeutic course but the true metabolic rate has stayed constant, PVE may cause an erroneous decrease in SUV. Conversely, if a tumor is small at the beginning but increases in size over the course of therapy, then SUV will erroneously appear to increase, even if the true metabolic rate decrease or remain constant. For these reasons, using SUVs as a semi-quantitative index in the follow-up studies has to be interpreted with caution especially in small tumor.

The results from the present study showed that SUV$_{max}$ at different scan durations (3, 5, 10, 15 and 20 minutes) were homogeneity. Therefore, increasing the emission scan duration from 3 to 20 minutes did not affect SUV. These results agreed with Visvikis et al(8). They reported that the bias on the SUV decreased by less than 15% when the emission scan duration changed from 15 to 5 minutes. Feuardent et al(7) found that changes in SUV were never more than 5% when changing emission acquisition from 6 to 18 minutes. Lengthening emission scan duration can be allowed for better image contrast while SUV dose not change.

Conclusion

The present research showed that the number of iterative updates affected both SUV$_{avg}$ and SUV$_{max}$. Higher number of iterative updates introduced image noise leading to higher SUV. The optimal number of iterative updates that compromised between image noise and resolution was 64. Tumor size and tumor-to-background ratio (TBR) also affected SUV. The percentages of underestimation of SUV were higher in small size tumor than the large one. Higher TBR yielded higher underestimation of SUV. Finally, scan duration or preset time did not affect SUV.

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ปัจจัยที่มีผลกระทบต่อค่า standardized uptake value (SUV) ของการถ่ายภาพ positron emission tomography (PET) ด้วย ^{18}F-FDG

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วัตถุประสงค์: *วัตถุประสงค์ของการศึกษานี้เพื่อศึกษาปัจจัยที่มีผลกระทบต่อค่า SUV ในการถ่ายภาพ PET ด้วย* ^{18}*F-FDG*

วัสดุและวิธีการ: *เครื่อง PET/CT Biograph 64 ถูกนำมาใช้ในการเก็บข้อมูล หุ่นจำลอง NEMA PET ซึ่งประกอบด้วยทรงกลม 6 ขนาด โดยมีเส้นผ่านศูนย์กลางตั้งแต่ 10 ถึง 37 มิลลิเมตร ถูกนำมาใช้เพื่อจำลองร่างกายมนุษย์และก้อนมะเร็ง ค่าความแรงรังสีของ* ^{18}*F ในแบ็คกราวด์ที่ใส่ในหุ่นจำลองมีค่าเท่ากับ 0.14* μ*Ci/ml และอัตราส่วนความแรงรังสีระหว่างก้อนมะเร็งและแบ็คกราวด์ (ทีบีอาร์) ที่ 2:1, 5:1 และ 10:1 ถูกนำมาศึกษา ในแต่ละทีบีอาร์ใช้เวลาในการเก็บข้อมูล 3 นาที และเก็บทั้งหมด 30 ไซโนแกรม ทำการศึกษาเวลาในการถ่ายภาพที่ต่างกันเริ่มจาก 3 นาที ถึง 20 นาที โดยใช้ทีบีอาร์ที่ 5:1 และในแต่ละเวลาถ่ายภาพจะทำการเก็บข้อมูล 3 ครั้ง ไซโนแกรมจะถูกนำมาสร้างภาพด้วย Order Subset Expectation Maximization (OSEM) พร้อมกับ 5 mm Full-Width-at-Half-Maximum (FWHM) Gaussian filter ไซโนแกรมที่ค่า TBR เท่ากับ 5:1 ถูกนำมาสร้างภาพโดยเปลี่ยนจำนวนการปรับเทียบของ OSEM (N) ตั้งแต่ 8 ถึง 168 และวัดค่า* SUV_{avg} *และ* SUV_{max} *เปอร์เซ็นต์การประเมินค่าต่ำกว่าความจริงของ SUV จะถูกนำมาใช้ใน การศึกษาผลของขนาดก้อนมะเร็งและทีบีอาร์ intraclass correlation coefficient (ICC) ถูกนำมาใช้ในการทดสอบ ความน่าเชื่อถือของ* SUV_{max} *ที่ได้จากการใช้ช่วงเวลาในการถ่ายภาพต่างกัน*

ผลการศึกษา: *ผลที่ได้แสดงให้เห็นว่าทั้ง* SUV_{avg} *และ* SUV_{max} *จะเพิ่มขึ้นอย่างรวดเร็วตามจำนวน N เมื่อ N น้อยกว่า 48 และเพิ่มขึ้นเล็กน้อยหลังจากนั้น เมื่อเปลี่ยนค่าทีบีอาร์จาก 2:1 ถึง 10:1 สำหรับทรงกลมขนาด 37 มิลลิเมตร เปอร์เซ็นต์ การประเมินค่าต่ำกว่าความจริงของ* SUV_{max} *และ* SUV_{avg} *มีค่าอยู่ในช่วง 8.17% ถึง 22.46% และ 41.44% ถึง 52.23% ตามลำดับ และสำหรับทรงกลมขนาด 10 มิลลิเมตร มีค่าอยู่ในช่วง 40.38% ถึง 54.52% และ 48.97% ถึง 67.73% ตามลำดับ เมื่อเปลี่ยนช่วงเวลาในการถ่ายภาพจาก 3 ไปถึง 20 นาที ความน่าเชื่อถือของ* SUV_{max} *มีค่า ICC เท่ากับ 0.966*

สรุป: *โดยสรุปค่า SUV จะเพิ่มขึ้นตามจำนวน N เปอร์เซ็นต์การประเมินค่าต่ำกว่าความจริงของ SUV จะขึ้นกับขนาดของก้อนมะเร็งและทีบีอาร์ ระยะเวลาในการถ่ายภาพไม่มีผลต่อค่า SUV*