Developing an application to support cancer diagnosis based on standardized uptake value

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ABSTRACT

Positron emission tomography (PET) is a type of nuclear medicine procedure that measures the metabolic activity of cells in body tissues that is well suited for detecting, staging and monitoring malignant tumours. The use of PET as a prognostic indicator based on Standardized Uptake Value (SUV) is a powerful tool to supplement the visual interpretation used by physicians. However, when scientists need to conduct desired research, they may face significant difficulties if they have no access to the vendor's application. In this paper, the authors have successfully developed the application based on the algorithm that they proposed. The maximum and average SUV of slices calculated from the authors' application are directly compared with the results from Inobitec DICOM Viewer program and the accuracy is, respectively, 85.4% and 88.7%.

Keywords: Positron Emission Tomography combined Computed Tomography (PET/CT); Standardized Uptake Value (SUV); Digital Imaging and Communication in Medicine (DICOM).

1. INTRODUCTION

SUV, defined as retention normalized to the injected dose and patient body weight, is an established index for quantifying glucose metabolic activity in tissues [1]. Several studies have been conducted on this topic, with the majority of them focusing on the role of SUV in the clinical diagnosis process such as in [1-3]. To be more specific, Paul E. Kinahan asserted that SUVs are now commonplace in clinical and have a specific role in assessing patient response to cancer therapy. He and his colleagues performed a research [2] review on the overall imaging process and estimates of the magnitude of errors, where known, are given. They also provided recommendations for best practices in improving SUV accuracy.

While others primarily worked on the SUV calculation and calibration process like in [4-6]. Such as the study was done by Han-Back Shin and his colleagues [4] on the conversion procedure for SUV calculations. By using the NEMA IEC Body phantom and Allegro PET scanner, they conducted measurements and performed calculations by using commercial software and the proposed self-developed program, respectively, to compare the SUVs by using conversion data. The outcome of the research suggests a simple and convenient method to solve the incompatibility with the SUVs of self-developed program and commercial one was lower than 20%. This is not suitable as, in reality, many vendors are taking part in the PET/CT imaging process and this could cause a lot of trouble

In addition, some research was conducted on how to reproduce the values after a certain time or on the aspect of bias and the influence of image noise on single-pixel SUV persistence such as [7, 8]. Martin A. Lodge, Muhamand A. Chaudhry, and Richard L. Wahl carried out a study [7] to evaluate the aspects of bias and the influence of image noise on single-pixel SUV persitance. They analyzed reproducibility and bias using 3-dimensional PET data acquired for 15 minutes in a single bed position in twenty different 18F-FDG oncology patients. They came to the

conclusion that images with noise properties typically associated with clinical whole-body studies, peak SUVs, provide a slightly more robust alternative for assessing the most metabolically active region of a tumor.

A lot of groundwork has been laid with those explorations focusing on the process of calculating SUV. However, they all came up with similar problems due to not taking the differences between PET/CT scan device manufacturers into consideration, which hampered the process in reality. Furthermore, further research on the application of SUV is not possible without the manufacturer's application. This creates huge obstacles for the operation and makes it nearly impossible to adjust appropriately since all the vendor's calculations are kept secret.

Hence, the aim of this article is to propose a calculation scheme and algorithm based on image intensity to calculate SUV for PET/CT image data standardized under the DICOM standard from different vendors.

2. BACKGROUND INFORMATION

2.1. Basic structure of DICOM file

DICOM stands for Digital Imaging and Communications in Medicine is the international standard for medical images and related information. It defines the formats for medical images that can be exchanged with the data and quality necessary for clinical use. Basic tructure of a DICOM file shown in figure 1.

DICOM files usually consist of two main parts: DICOM Header and DICOM Data. DICOM Header includes 3 parts: File Preamable, DICOM Prefix and File Meta Information. The Header usually stores some of the following information:

- Patient’s information.
- Time of capture information.
- Information about the device that generated the image.

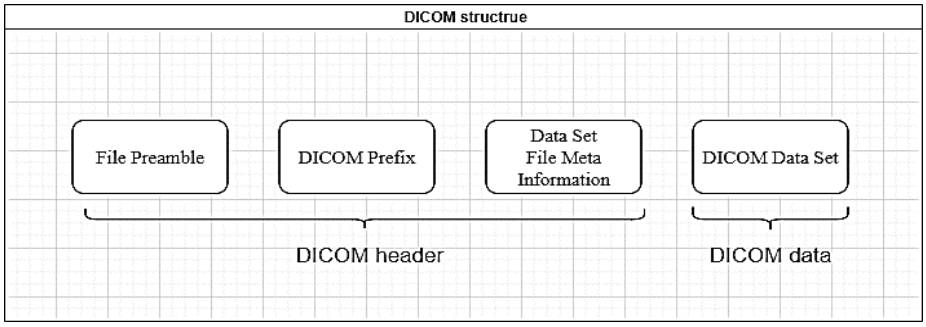

Figure 1. *Basic structure of a DICOM file.*

DICOM Data is made up of multiple DICOM Data Set. Each DICOM Data Set consists of many Data Elements which include: Tag, VR (optional), Value Length, Value Field

2.2. Standardized Uptake Value

SUV, also known as Standardized Uptake Value, is a simple way of determining activity in PET imaging, most commonly used in fluorodeoxyglucose (FDG) imaging. As the name suggests it is a mathematically derived ratio of tissue radioactivity concentration at a point in time and administered dose divided by body weight.

SUV is used as a measurement of relative tissue/organ uptake facilitates comparisons between patients, and has been suggested as a basis for diagnosis. Usually, it is used to separate tissues characterized as benign or malignant using SUV thresholds.

The basic expression for SUV, according to research [9] is:

$$SUV_{BW} = \frac{AC}{D/BW} \quad (1)$$

Whereby: - AC: Radioactive activity concentration [Bq/cc] measured by the PET scanner within a region of interest (ROI);

- D: Injected radiolabeled FDG [Bq] dose at a specific time;
- BW: Weight of the patient [kg].

3. PROPOSED ALGORITHM

3.1. Details of the algorithm

The authors proposed an algorithm to calculate SUV based on Formula (1) including 4 steps that can be divided into 2 phases.

- Phase 1: Extract, convert and adjust necessary data;
- Phase 2: Calculate SUVs for ROI that has MxN size.

3.1.1. Algorithm for phase 1

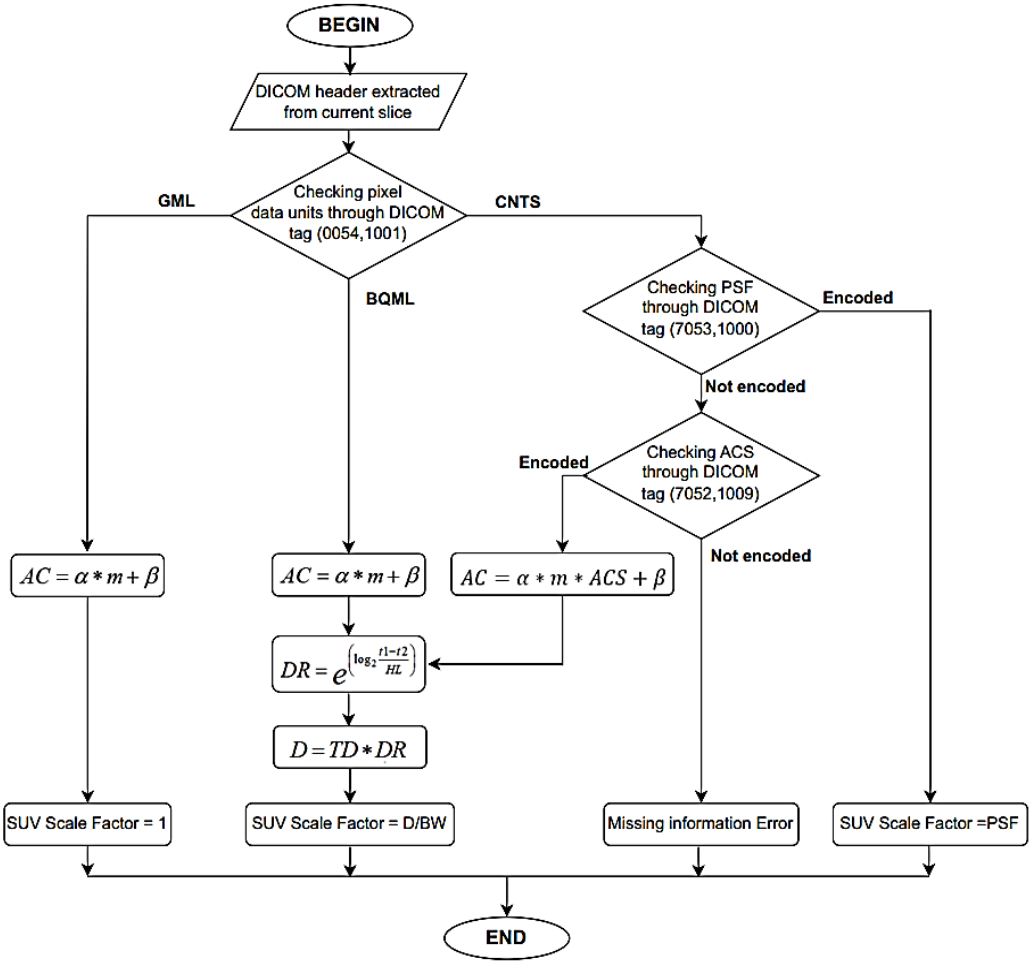

Figure 2. *Algorithm for phase 1: Extract, convert and adjust data.*

The Algorithm for phase 1 is illustrated in figure 2. This phase includes the following steps:

- Step 1: *Choosing ROI*. In this reasearch, the authors choosed ROI as the entire slice.
- Step 2: Convert pixel value into radioactive activity concentration using equation (2).

$$AC = \alpha * m + \beta \quad (2)$$

Where: - AC: Activity concentration in ROI during recorded time [Bq/cc];
- α: Rescale slope;
- β: Rescale intercept;
- m: Original pixel intensity.

Rescale slope (stores in tag (0028,1053)) and rescale intercept (stores in tag (0028,1052)) allow transformation of pixel values to other units, as specified in the Units (stores in tag (0028,0054)) tag. Those values are determined by the manufacturer of the hardware.

Units tag (0054,1001) will be one of the three following values: "GML, BQML, or CNTS":

- GML (Gram/millimeter): this value is usually seen with PET images recorded by GE Medical PET/CT scan device. In this case, SSF, according to the manufacturer, will equal to 1.

- BQML (Becquerels/millimeter): this is the most common unit of "Units" tag for PET images. In this case, we will convert AC according to equation (2) in order to calculate SUVs.

- CNTS (Counts): This value is unique for PET images produced by Phillips PET/CT scan devices. When encountering this, we need to orderly check tag (7053,1000) and (7053, 1009). If tag (7053,1000) exists, SSF value is equal to PSF. If tag (7053, 1009) exists, we will have to convert AC due to the following equation:

$$AC = \alpha * m * ACS + \beta \quad (3)$$

According to document [10] Phillips claims that only with Phillips private attribute can a physician calculate SUVs in the correct way. Therefore, in some circumstances, SUVs might be unable to be calculated due to the missing of two private tags (7053, 1000) and (7053, 1009).

- Step 3: *Calculate SUV scale factor (SSF).* For convenience during information process and storing, we call:

$$SSF = \frac{BW}{D} \quad (4)$$

With: BW will be extracted from DICOM tag (0010,1030) and D in equation (4) can be calculated using the following equation:

$$D = TD * DR \quad (5)$$

Where: - D: Administered dose at recorded time [Bq].
- TD: Total Dose - total dose of radionuclide injected into the patient [Bq].
- DR: Decay Ratio - radiation decay time, calculated by the following equation:

$$DR = e^{\left(\log_2 \frac{t1-t2}{HL}\right)} \quad (6)$$

Where: - t1: Scan Time or time that the PET/CT device starts to record image usually equals to Series Time (stores in tag (0008, 0031)) [s];
- t2: Start Time or time that radionuclide was injected into patient usually equal to Radiopharmaceutical Start Time (stores in (0018,1072))[s];
- HL: The half-life of a radioactive isotope, extracted from tag (0018,1075) [s].

3.1.2. Algorithm for phase 2

The second phase, with algorithm shown in figure 3, is the repetition of the following step:

- Step 4: Calculate SUVs. We will calculate SUV for 1 image pixel base on equation (1) and (4) which now become:

$$SUV = AC * SSF \quad (7)$$

Following that, we will calculate the SUV of each pixel one by one. Starting from the top left corner it will be the origin of the coordinates, which is (0,0). Then, we will calculate SUVs for the next pixel, from left to right, top to bottom, until the very last pixel by repeating step 4.

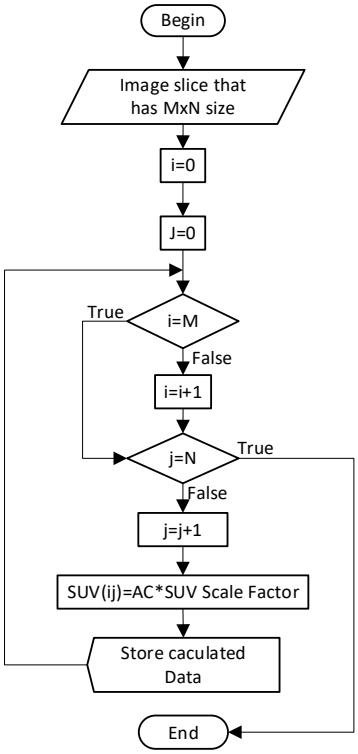

Figure 3. *Algorithm for phase 2: Calculate SUVs for ROI that has MxN size.*

3.2. Algorithm of Decay Ratio calculation

Decay Ratio (DR) - radiation decay time, calculated by the equation (6). To calculate the DR, it is necessary to determine Scan Time (t1) and Start Time (t2). In the process of extracting t1 and t2, document [10] propose that t1 is equal to Series Time (0008, 0031) and t2 is equal to Radiopharmaceutical Start Time (0018, 1072).

3.2.1. Scan Time calculation

Algorithm for handling Scan Time is shown in figure 4. If Series Time (0008, 0031) is sooner than Acquisition Time (0008, 0022), t1 is equal to Series Time (0008, 0031). In cases where Series Time (0008, 0031) is later than Acquisition Time (0008, 0022), we have different handles. With GE medical device, t1 in this circumstance is equal to GE Private Scan Time which can be extracted from tags (0009, 0100d). If the image is not recorded by GE scanning device, or does not have the private tag (0009, 0100d), we will check on Frame Reference Time (0054, 1300) and Actual Frame Duration (0018, 1242). If those tags are empty, we will have to find the earliest Acquisition Time (0008, 0032) among the slices in the same study. In this case, we call it ATE. Then t1 is equal to this value. In cases where Frame Reference Time (0054, 1300) and Actual Frame Duration (0018, 1242) exist, we will calculate t1 by this formula:

$$t1 = AT - \frac{FRT}{1000} + ACT \tag{8}$$

Where: - AT: Acquisition Time (Stores in tag (0008, 0022)) (s);

- FRT: Frame Reference Time (Stores in tag (0054, 1300)) (s);

- ACT: Average count rate within frame, can be calculated by formula (9):

$$ACT = \frac{1}{DC}\ln\left(\frac{DDF}{1-e^{DDF}}\right) \quad (9)$$

- DDF: Decay during frame;
- DC: Decay constant calculated by the following formula:

$$DC = \frac{\ln(2)}{HL} \quad (10)$$

- HL: The half-life of a radioactive isotope, stored in (0018,1075) tag [s];
- DDF is calculated by using the formula:

$$DDF = DC * FD \quad (11)$$

- FD: Frame duration calculated by:

$$FD = \frac{AFD}{1000} \quad (12)$$

- AFD: Actual Frame Duration (stores in tag (0018, 1242)).

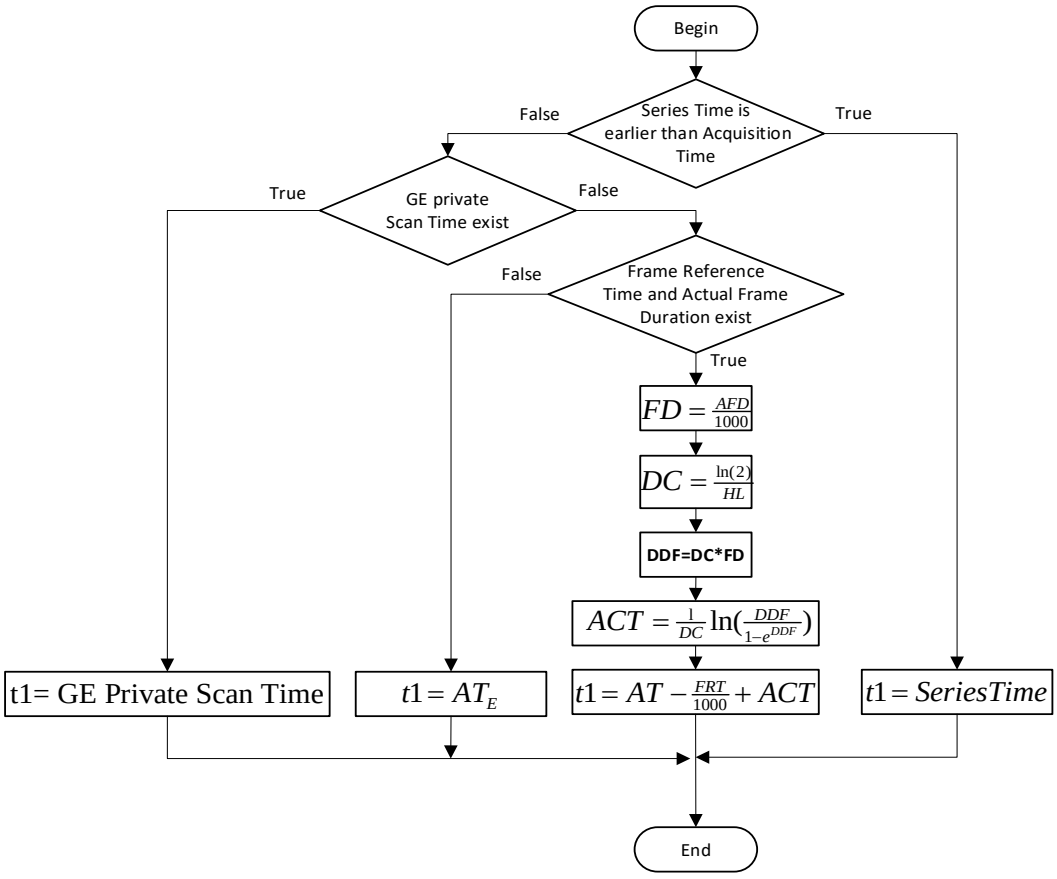

Figure 4. *Algorithm for handling Scan Time.*

3.2.2. Start time calculation

With t2, determined by algorithm shown in figure 5, first we will check on tag (0018,1078) representing the Radiopharmaceutical Start Date Time. t2 is equal to the time extracted from (0018,1078) tag.

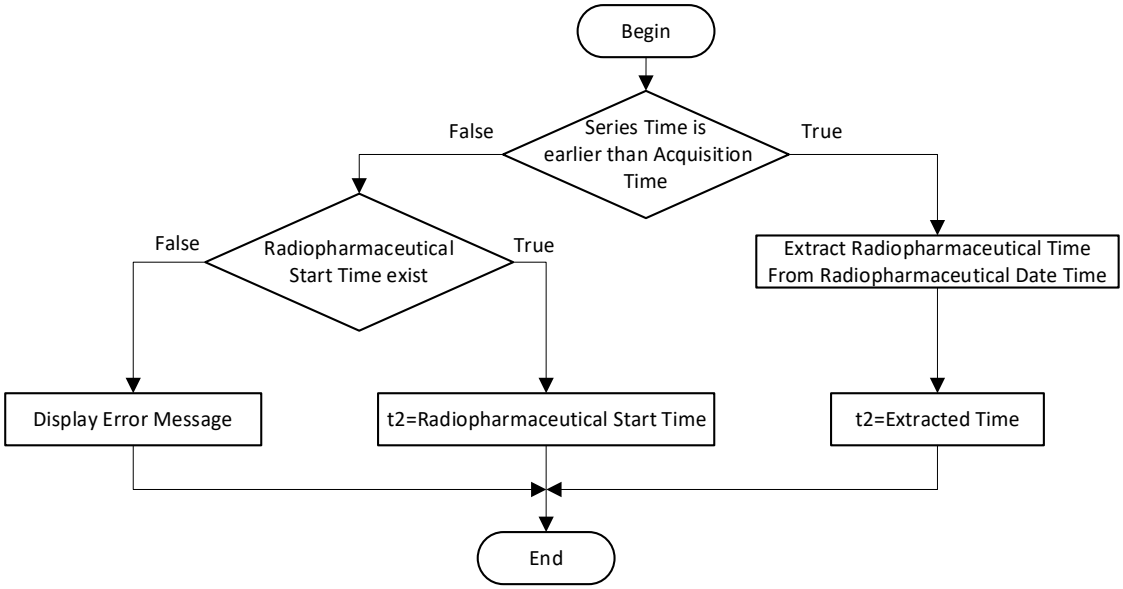

Figure 5. *Algorithm for handling Start Time.*

4. APPLICATION DEVELOPMENT AND EVALUATION

4.1. Application development

The authors have built a program to calculate SUVs using the Python application. Graphical User Interface of the application is shown in figure 6. The application has 7 sections which can be divided into 3 main parts.

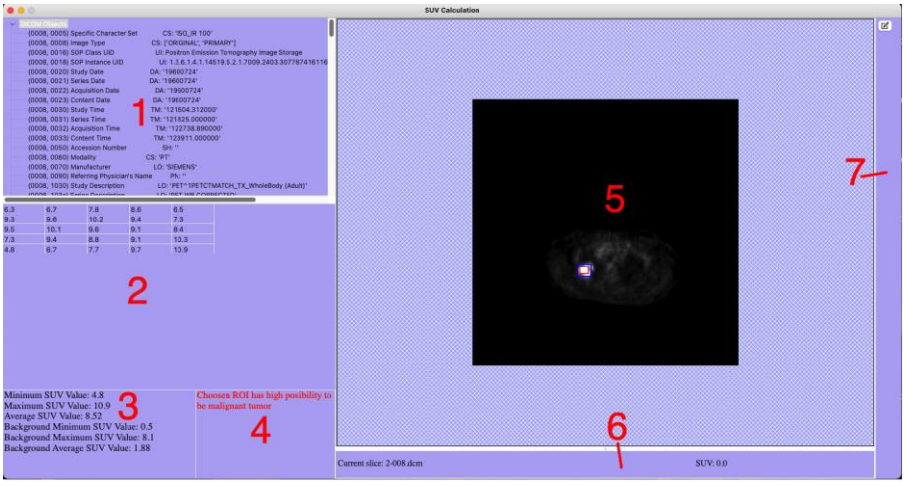

Figure 6. *Graphical User Interface of the application.*

- The first part includes: section 1, section 2, section 3, and section 4. This part is the information display part of the application:

- Section 1 will display all the information stored in DICOM Header.
- Section 2 will display in detail the SUVs of ROI selected by the user.
- Section 3 will display Maximum, Minimum, Average SUVs of the selected ROI.
- Section 4 will display the application conclusion on status of the selected ROI. The color of the text also displays the level of warning to users. "Red" indicates a highly suspect area of malignant tumor. "Yellow" indicates an area that has an abnormal metabolic process but cannot be diagnosed as a malignant one. "Green" indicates the normal area.

- The second part includes sections 5 and 6. This part will display images stored in DICOM files as well as display some other information.

- Section 5 will display image stored in DICOM file.

- Section 6 will display some extracted information and calculated SUVS of the specific pixel at the current mouse pointer.

- Third part includes section 7, which is the tools bar. This consists of the chosen ROI tools that the user can use to choose a suspicious region.

4.2. Result evaluation

The maximum and average SUVs of slices calculated from the application were directly compared with result from Inobitec DICOM Viewer program due to lack of access to applications created by PET/CT manufacturer. We used 2476 slices of DICOM files that were obtained from 12 patients taken through the PET/CT scanning. The results evaluation process included two steps:

- First step is to checking on correlation between the results received from Python with the reference one. This was completed using Pearson Correlation Coefficient.
- Second step is to calculate the accuracy of the results.

4.2.1. Pearson correlation test

Correlation between results are tested using Pearson Correlation Coefficient (r). Below is a formula for calculating the Pearson correlation coefficient (r):

$$r = \frac{n\sum xy - \left(\sum x\right)\left(\sum y\right)}{\sqrt{\left[n\sum x^2 - \left(\sum x\right)^2\right]\left[n\sum y^2 - \left(\sum y\right)^2\right]}} \tag{13}$$

With:

- x and y are the two objects that we need to measure the statistical relationship. x are results from Python scheme and y are results from Inobitec;

- n is the number of sample.

Table 1. *Correlation of maximum SUVs between 2 systems.*

		Python	**Inobitec**
Python	Pearson Correlation	1	0.863(**)
	Sig.(2-tailed)	.	.000
	Number of Samples	2476	8476
Inobitec	Pearson Correlation	0.863(**)	1
	Sig.(2-tailed)	.000	.
	Number of Samples	2476	2476

*** Correlation is significant at the 0.01 level (2-tailed).*

Table 2. *Correlation of average SUVs between 2 systems.*

		Python	**Inobitec**
Python	Pearson Correlation	1	0.893(**)
	Sig.(2-tailed)	.	.000
	Number of Samples	2476	2476
Inobitec	Pearson Correlation	0.893(**)	1
	Sig.(2-tailed)	.000	.
	Number of Samples	2476	2476

*** Correlation is significant at the 0.01 level (2-tailed).*

The result for both maximum ad average value indicates a close correlation.

4.2.2. Accuracy

The accuracy percentage of SUV was calculated using the following formulas:

$$A = 100\% - ER \tag{14}$$

$$ER = \frac{|OV - AV|}{AV} * 100 \tag{15}$$

Where: - ER: Error Rate (%);

- OV: Observed Value, in this case is the value received from Python scheme;

- AV: Actual Value, in this case the authors assume it was the results received from Inobitec's Software.

The accuracy percentages of maximum and average SUVs respectively, are 85.4% and 88.7%.

5. CONCLUSIONS

As has been demonstrated in this paper, the authors have presented all the related problems during the process of calculating SUV. Through the use of rigorous methodologies and data analysis techniques, the results show that the software can be used to calculate the necessary values for cancer diagnosis. Our research has provided important insights into the topic, creating a simpler and more convenient way to further research SUV calculation, with accuracy percentages of maximum and average values of 85.4% and 88.7%, respectively. While there may be limitations to our research, such as sample size or methodology, we believe that our findings offer valuable contributions.

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TÓM TẮT

Phát triển phần mềm hỗ trợ chẩn đoán ung thư dựa trên chỉ số hấp thụ hoạt chất phóng xạ chuẩn

Chụp cắt lớp phát xạ positron (PET) là một quy trình y học hạt nhân có khả năng thể hiện được hoạt động trao đổi chất của các tế bào trong cơ thể và là công cụ rất phù hợp để phát hiện, phân loại và theo dõi các khối u ác tính. Việc sử dụng PET như một công cụ định lượng dựa trên Chỉ số hấp thụ hoạt chất phóng xạ chuẩn (SUV) là một công cụ rất hữu ích cho các bác sĩ. Tuy nhiên, trong trường hợp cần tiến hành nghiên cứu, họ có thể gặp tương đối nhiều khó khăn nếu không sử dụng phần mềm đi kèm của nhà sản xuất thiết bị PET. Trong bài báo này, nhóm tác giả đã phát triển thành công ứng dụng dựa trên thuật toán của chính nhóm tác giả đề xuất. Giá trị SUV tối đa và trung bình của các slice ảnh tính toán từ ứng dụng của nhóm tác giả được so sánh trực tiếp với kết quả từ chương trình Inobitec DICOM Viewer và độ chính xác lần lượt là 85,4% và 88,7%.

Từ khoá: Chụp phát xạ cắt lớp positron kết hợp chụp cắt lớp vi tính (PET/CT); Chỉ số hấp thụ hoạt chất phóng xạ chuẩn (SUV); Chuẩn truyền thông hình ảnh kỹ thuật số trong y tế (DICOM).