Heliyon 10 (2024) e37299

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Evaluating the accuracy of planar gated blood pool processing software using simulated patient studies

H. Pieters [a,*], J.A. van Staden [b], H. du Raan [b], M.G. Nel [c], G.H.J. Engelbrecht [c]

[a] Nuclear Medicine Unit, Klerksdorp/Tshepong Hospital Complex, Klerksdorp, 2571, South Africa
[b] Department of Medical Physics, University of the Free State, Bloemfontein, 9301, South Africa
[c] Department of Nuclear Medicine, Universitas Academic Hospital, Bloemfontein, 9301, South Africa

A B S T R A C T

Planar gated blood pool (GBP-P) radionuclide imaging is a valuable non-invasive technique for assessing left ventricular ejection fraction (LVEF). Serial cardiac imaging can be performed to monitor the potential decline in LVEF among patients undergoing cardiotoxic chemotherapy. Consequently, accurate LVEF determination becomes paramount. While commercial software programs have enhanced the LVEF values' reproducibility, concerns remain regarding their accuracy. This study aimed to generate a database of GBP-P studies with known LVEF values using Monte Carlo simulations and to assess LVEF values' accuracy using four commercial software programs.

We utilised anthropomorphic 4D-XCAT models to generate 64 clinically realistic GBP-P studies with Monte Carlo simulations. Four commercial software programs (Alfanuclear, Siemens, General Electric Xeleris, and Mediso Tera-Tomo) were used to process these simulated studies. The accuracy and reproducibility of the LVEF values determined with these software programs and the intra- and inter-observer reproducibility of the LVEF values were assessed.

Our study revealed a strong correlation between LVEF values calculated by the software programs and the true LVEF values derived from the 4D-XCAT models. However, all the software programs slightly underestimated LVEF at lower LVEF values. Intra- and inter-observer reliability for LVEF measurements was excellent.

Accurate LVEF assessment is crucial for determining the patient's cardiac function before initiating and during chemotherapy treatment. The observed underestimation, particularly at lower LVEF values, emphasises the need for the accurate and reproducible determination of these values to avoid excluding suitable candidates for chemotherapy. The software programs' excellent intra- and inter-observer reliability highlights their potential to reduce subjectivity when using the semi-automatic processing option.

This study confirms the accuracy and reliability of these commercial software programs in determining LVEF values from simulated GBP-P studies. Future research should investigate strategies to mitigate the underestimation biases and extend findings to diverse patient populations.

Gated blood pool studies, left ventricular ejection fraction, Monte Carlo simulations, 4D-XCAT models.

1. Introduction

Planar gated blood pool radionuclide imaging (GBP-P) has long been instrumental in non-invasive assessments of regional wall motion, left ventricular ejection fraction (LVEF), and other indices of ventricular function [1]. LVEF, expressed as a percentage, represents the ratio of blood volume ejected during systole (stroke volume) from the left ventricle (LV) to the total volume of blood at the end of diastole. The primary modalities used for determining LVEF include GBP-P imaging, 2D/3D echocardiography (EC), and cardiac magnetic resonance imaging (CMR) [2–4]. While 2D/3D EC does not involve radiation exposure, it is less favoured due to its operator dependency and reliance on geometric assumptions [2–5]. CMR is often the standard choice for non-invasive cardiac studies

* Corresponding author.
E-mail address: pietersh24@gmail.com (H. Pieters).

https://doi.org/10.1016/j.heliyon.2024.e37299
Received 12 October 2023; Received in revised form 29 August 2024; Accepted 30 August 2024
Available online 2 September 2024

due to its superior contrast, resolution, and lack of radiation exposure [2,4,6]. However, CMR is unsuitable for patients with certain implants, such as implantable cardioverter defibrillators, most pacemakers, and metallic or cochlear implants, which may contraindicate its use [2,4,5].

Since the 1970s, GBP-P imaging, a cost-effective, non-invasive, and reproducible procedure to determine LVEF in patients, has gained popularity in evaluating cardiac ventricular function [7,8]. The European Association of Nuclear Medicine (EANM) guidelines provide reference LVEF values for radionuclide imaging of cardiac function [9]. LVEF is widely used to assess the risk of cardiotoxicity in chemotherapy patients [2–5,8,10–16]. It is widely agreed that chemotherapy treatment is discontinued if the pre-chemotherapy LVEF is below 50 % or decreases by more than 10 % post-treatment [17]. Accurate and reliable LVEF measurements are thus essential for optimal patient care, preventing complications [2,3,7,8,10].

Sachpekidis et al. and Foley et al. [4,5] have highlighted GBP-P's distinct advantages, including ease of use, high accuracy, and reproducibility, compared to CMR imaging. Their findings underscore GBP-P's potential as a robust technique for non-invasive LVEF assessment, emphasising its value in clinical practice and research settings [4].

Commercial software programs are frequently used to process GBP-P studies to determine LVEF values. Software updates, including semi-automatic and automatic processing methods, have improved the reliability of these measurements by reducing the risk of variance. These advancements aim to enhance the accuracy and consistency of LVEF calculations. However, ensuring the accuracy and precision of LVEF values obtained from new and existing software remains crucial for delivering consistent, accurate and reliable results [10]. Fair et al. [11] and De Bondt [15] have noted that software programs often lack extensive testing before clinical implementation.

Validating the accuracy and consistency of commercial software for LVEF measurement using human and/or animal GBP-P studies faces challenges, particularly concerning ethical considerations, radiation exposure, and difficulties in obtaining known cardiac volumes for verification. While physical phantoms offer a controlled testing environment, they have limitations in replicating the complex anatomy of human organs and are costly to produce in various sizes [15,18].

To address these challenges, the emergence of digital hybrid phantoms provides an opportunity to evaluate and compare the accuracy of LVEF values determined with various software packages by comparing it with known input values. We therefore propose using a clinically realistic, Monte Carlo (MC) simulated database of GBP-P images with known LV volume and LVEF values for software validation. This approach overcomes the ethical and practical limitations of human and animal studies and the constraints associated with physical phantoms.

In a previous study [13], we proposed using hybrid phantoms to simulate GBP studies. Specifically, we utilised the 4D-XCAT phantom, developed by Segars et al. [19,20] for the evaluation of LVEF values using commercial software. The XCAT software enables the creation of digital patient phantoms with detailed anatomical and physiological realism [20] useful for biomedical research [21]. It includes a diverse population of human anatomies, enhancing phantom variability by varying age, height and weight [21–23]. The 4D-XCAT phantom is a valuable resource in imaging research for assessing imaging devices and techniques.

1.1. This study aims to

(i) Generate a database of GBP-P studies with known LVEF values using MC simulations of digital hybrid patient phantoms.
(ii) Evaluate the accuracy of LVEF values obtained from processing the simulated GBP-P studies using four commercial software programs.

2. Materials and methods

2.1. 4D-XCAT models and Monte Carlo simulations

A database of six anthropomorphic 4D-XCAT models (three male- and three female models) [19] was used to simulate clinically realistic GBP-P studies [13] with the SIMIND MC program [24]. These models were selected to include a wide range of ventricular end-diastolic (ED), end-systolic (ES), and stroke volumes, thereby providing a comprehensive set of LVEF values. The accuracy of four commercially available software programs for determining LVEF values was assessed using the simulated GBP-P studies. Detailed demographic information regarding the selected 4D-XCAT models is presented in Table 1.

Each of the six 4D-XCAT models was scaled to create a database with additional models with varying ES cardiac volumes, resulting in a range of EF values. Cardiac scaling factors were applied to generate different clinically realistic phantoms. Fig. 1 illustrates a

Table 1
Demographic and biometric data of the six 4D-XCAT models.

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Gender	Male	Female	Male	Female	Male	Female
Age	36	59	52	54	60	51
Ethnicity	Caucasian	Caucasian	Caucasian	Unknown	African	Unknown
Weight (kg)	75.60	63.70	108.00	87.00	81.50	59.25
Height (cm)	176.1	162.7	183.2	161.0	175.0	158.0
Body Mass Index	24.38	24.06	32.18	33.56	26.61	23.73

flowchart of the database generation. Left and right ventricular as well as atrial volumes were kept in clinically acceptable ranges [25], and models not complying were excluded.

A summary of the parameters used to create the 4D-XCAT models is as follows.

- All models were generated to include cardiac and respiratory motion [19,21–23]. The entire heart was translated and/or rotated to mimic respiratory motion.
- Thirty-two time-frames were generated over the cardiac cycle for all models, as stated by guidelines [9,26,27] implemented at our institution.
- No other scale factor was introduced to any of the organs besides the heart scale factor.
- Segmented activity maps and the density maps used for the simulation were generated as 512 x 512 image matrixes with a voxel size of 0.98 × 0.98 × 0.98 mm^3 (Fig. 2).

The Siemens Symbia gamma camera model used to simulate the GBP-P studies was described in our previous article [13]. The XCAT software was used to create 32 time-frames of the 4D-XCAT phantom for each patient model. Due to factors such as breathing, cardiac rotation, and the fluctuating cardiac cycle, the heart's position within the thoracic cavity changes at each of the 32 time-frames. The attenuation- and activity maps generated with the XCAT software for the 32 time-frames of the 4D-XCAT models served as input files for the SIMIND MC code. The phantoms' activity distributions (also referred to as activity maps) were derived from GBP-P studies of patients from our clinic. The simulations were performed with the assistance of the High-Performance Cluster of the University of the Free State with 280 kcounts per time frame for 200 million photon histories per image to limit the MC statistical uncertainty. As recommended by Ljungberg [13,24,28], Poisson noise was incorporated during the simulation process to ensure the noise levels in the simulated images closely resembled those observed in clinical radionuclide images. Other simulation parameters are summarised in the flowchart in Fig. 1.

The 32 simulated time-frames were concatenated using ImageJ [29] to create GBP-P studies of ~9000 kcounts mimicking clinically realistic GBP-P studies. These simulated studies (Fig. 3) were subsequently converted to DICOM file format using an in-house software program and transferred to the appropriate Nuclear Medicine processing workstations.

2.2. Processing the simulated GBP-P studies

Four different commercial software programs (Alfanuclear (AN), Xeleris by General Electric (GE-X), Siemens (SM), and Tera-Tomo from Mediso (M-TT)) were utilised to process the 64 simulated GBP-P studies (Table 2, Fig. 1). Three independent operators with at least five years of clinical experience blindly processed each GBP-P study three times, allowing the assessment of intra- and inter-observer reproducibility of LVEF calculation. Bunting et al. [30] indicated that the time between repetitions should be long enough to prevent interference from the preceding test. For this reason, the operators in our study were asked to repeat the processing of the GBP-P studies on different days to ensure that the observers were not biased. All GBP-P studies underwent standard processing procedures similar to routine clinical studies. Any modifications to the semi-automated processing were made as required by the user (e.g., adjustment of the region of interest where the processing algorithm failed to accurately identify the left ventricle) (Fig. 3). The LVEF was calculated for all processing software after a background correction was applied to the LV counts obtained in the ED and ES phases (Table 2).

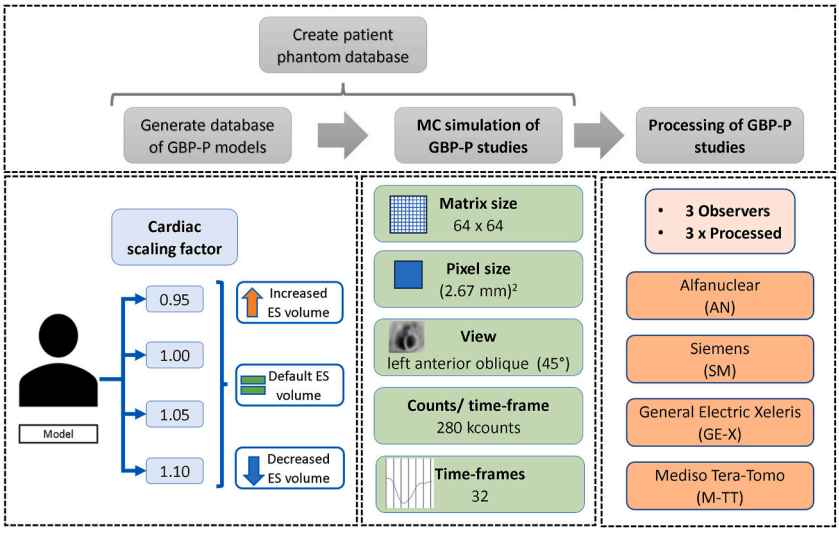

Fig. 1. Flowchart illustrating the creation of the patient phantom database by generating GBP-P models and MC simulation of the GBP-P studies. Processing of the GBP-P studies is also shown.

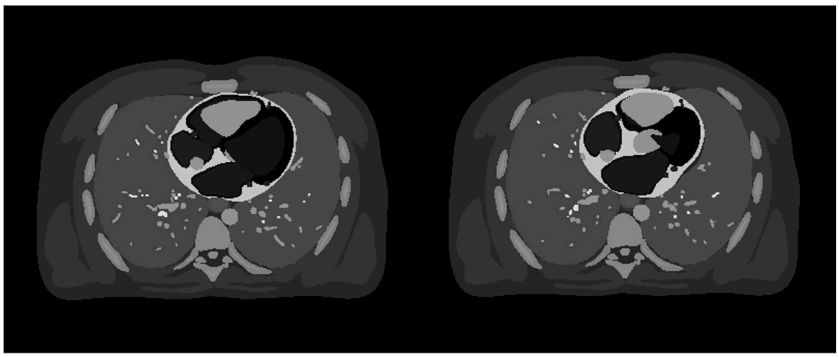

Fig. 2. Sample transaxial images of the 4D-XCAT phantom's segmented activity map during the end-diastolic (ED) and end-systolic (ES) phases.

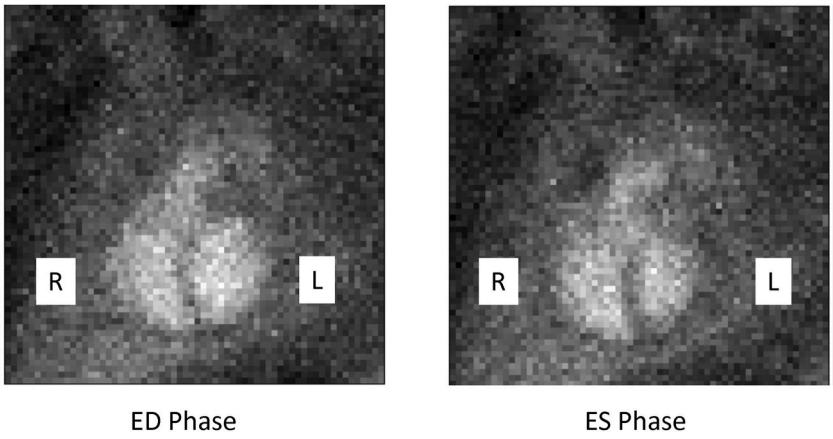

Fig. 3. Sample of MC simulated images of the ED- and ES-phase of the original 4D-XCAT model 1.

Table 2
Details of the four software programs used in this study.

Software	Company	Processing system	Manufacturing Address	Background ROI definition
AN	Alfanuclear	Data and Image Processor IM512P, version 2.0 [31]	Argentina	Manually drawn background ROI
SM	Siemens	Syngo workstation [32]	Germany	Automatically selected background ROI.
GE-X	General Electric	Xeleris [33]	United States	Automatically selected background ROI.
M-TT	Mediso	Tera-Tomo, version 3.07 [34]	Hungary	Manually drawn ROIs

3. Statistical analysis

LVEF mean and standard deviations of all the models were reported for the 4D-XCAT values and the AN-, SM-, GE-X-, and M-TT calculated values. A one-way analysis of variance (ANOVA) [35] test was performed in Excel to compare the LVEF values obtained with the four different software programs.

Linear regression analysis [30,36] and the Pearson correlation coefficients (R) [30,36] were used to evaluate the strength of the relationship and association between calculated LVEF values and the true (or absolute) LVEF values obtained from the 4D-XCAT models. The following guidelines regarding the correlation coefficient, proposed by Chan et al. [37], were used to assess the strength of the linear relationship: poor ($R < 0.3$), fair ($R = 0.3$–0.5), moderately strong ($R = 0.6$–0.8), and very strong ($R \geq 0.8$). The Standard Error of Estimate (SEE) measures the accuracy of the predictions made by the model [38], in this case, the processed LVEF values. The Data Analysis Toolkit in Excel [39] was used to perform regression analysis on the data and to determine the Pearson coefficient, SEE, and p – value.

Bland-Altman analysis [30,36] assessed the agreement between the LVEF values calculated with commercial software programs and 4D-XCAT models by plotting the difference between LVEF values against the true LVEF values. Any systematic trends in differences were also identified by Bland-Altman analysis. A p – value less than 0.05 indicated statistical significance for all statistical tests.

Inter- and intra-observer reliability was assessed by means of an Interclass Correlation Coefficient (ICC) [30,40] and coefficient of variation (CV) using the Real Statistics data analysis toolpack in Excel [41]. An ICC was also obtained to evaluate the agreement between the calculated LVEF using the different software (AN, SM, GE-X, M-TT) and the known 4D-XCAT values. ICC based on a 95 % confidence level was used, and the strength of agreement was assessed according to guidelines by Landis and Koch [42], which define agreement as poor (ICC <0.20), fair (ICC 0.21–0.40), moderate (ICC 0.41–0.60), good (ICC 0.61–0.80), or very good (ICC >0.80). Koo et al. [40] define an ICC >0.9 as excellent.

4. Results

4.1. 4D-XCAT models and Monte Carlo simulations

Table 3 displays the left ventricular ED- and ES volumes of the six original XCAT models and their corresponding stroke volumes.

Eight of the 72 4D-XCAT models were excluded due to inconsistencies and left ventricular ES volumes being too small compared to Kawel-Boehm's reference ranges [25]. The 64 4D-XCAT models used in this study had a range of ED volumes (159–78 ml), ES volumes (94–22 ml), and LVEF values (20–77 %)).

4.2. Left ventricular ejection fraction

The mean and standard deviation of the LVEF calculated from the ED and ES volumes of the 4D-XCAT phantoms as well as the LVEF values determined with the four commercial software programs from the simulated GBP-P studies, are presented in Table 4.

No significant difference was indicated between the LVEF values calculated by the four commercial software programs (one-way ANOVA test, $p = 0.64$). Furthermore, the agreement between the LVEF values for the 4D-XCAT and the four software programs was excellent (ICC $\geq$0.90, Table 5).

Linear regression analysis and Bland-Altman plots comparing the LVEF values of the four commercial software programs and the 4D-XCAT phantoms are shown in Fig. 4. The mean of the operators' data for each software program as well as their respective statistical analysis, are shown in Fig. 4.

The linear regression analysis showed that the agreement for LVEF values was very strong between 4D-XCAT and AN, SM, GE-X and M-TT ($R > 0.94$; $p < 0.1$) (Fig. 4(a)–(c), (e), (g)). The mean difference between the LVEF values for the 4D-XCAT and AN was -2.9 ± 7.9 %, between the 4D-XCAT and SM was -3.0 ± 7.8 %, between the 4D-XCAT and GE-X was -4.8 ± 9.2 % and -1.3 ± 10.6 % between the XCAT and M-TT (Fig. 4(b)–(d), (f), (h)).

4.3. Intra-/inter-observer reliability

No significant difference was indicated between the intra- ($p > 0.61$) and inter-observer ($p > 0.43$) reliability of LVEF values for the four software programs. The intra- and inter-observer reliability of AN, SM, GE-X, and M-TT, as assessed by ICC and CV, is shown in Table 6. Both intra- and inter-observer reliability was excellent for all the studied variables (ICC = 0.96–1.00). The CV ranged from 1.1 % to 5.8 % for intra-observer reliability and 3.2 %–6.6 % for inter-observer reliability.

5. Discussion

Our study successfully created a database of simulated GBP-P studies, demonstrating its utility as a valuable tool for assessing the performance of both new and existing cardiac processing software. The literature frequently highlights variations in LVEF calculations across different operators and software algorithms, primarily due to the lack of a known true LVEF value. In contrast, our study utilised known true LVEF values, allowing for a precise evaluation of the accuracy of various software packages.

The study uniquely assessed the accuracy of LVEF values obtained from four commercial software programs using MC-generated GBP-P studies. To our knowledge, this is the first investigation to specifically evaluate the accuracy and reproducibility of these programs in this context. By leveraging clinically realistic simulated studies, we could avoid the ethical and logistical challenges associated with involving human patients/volunteers.

Overall, the correlation between LVEF values obtained from simulated GBP-P studies and the true values calculated from the LV ED and ES volumes of the 4D-XCAT models was good. No significant difference was found between the LVEF values determined from the

Table 3
End-diastolic (ED)-, end-systolic (ES)-, and stroke volumes for the six original models.

	Left Ventricle Volumes (ml)			Right Ventricle Volumes (ml)		
Model number	**ED**	**ES**	**Stroke (ED – ES)**	**ED**	**ES**	**Stroke (ED – ES)**
1	136	71	65	102	71	31
2	109	43	66	82	49	33
3	158	62	97	119	71	48
4	96	37	58	71	43	29
5	117	46	71	87	52	35
6	90	35	55	67	40	27

Table 4
Known LVEF values for the 4D-XCAT models and calculated LVEF values obtained with the four commercial software programs: (AN: Alfa Nuclear; SM: Siemens, GE-X; General Electric Xeleris; M-TT: Mediso Tera-Tomo) presented as mean ± SD (n = 64).

LVEF	4D-XCAT	AN	SM	GE-X	M-TT
Mean (%)	53.7	50.8	50.7	48.9	52.4
Standard Deviation (%)	13.0	14.5	15.3	15.8	15.5

Table 5
Intra-class correlation for LVEF values between XCAT and the four processing software programs (AN: Alfa Nuclear; SM: Siemens, GE-X; General Electric Xeleris; M-TT: Mediso Tera-Tomo). Interclass correlation coefficients (ICC) with 95 % confidence interval.

		Intra-class correlation between XCAT and the different software			
		AN	SM	GE-X	M-TT
All Operators	ICC	0.94	0.94	0.90	0.93
	95 % Cl	0.90–0.96	0.90–0.96	0.84–0.94	0.88–0.95

simulated GBP-P studies and the true values calculated from the 4D-XCAT models. However, Bland-Altman analysis revealed a slight underestimation of LVEF values by all four software programs at lower LVEF values. This underestimation is consistent with previous reports and may result from factors such as underestimating the background activity in physical phantoms or self-attenuation of activity in patients with dilated ventricles [43].

The clinical importance of accurate and reliable LVEF values cannot be overstated, particularly in managing chemotherapy patients. The commonly accepted threshold for discontinuing chemotherapy is an LVEF value below 50 %. Therefore, the observed bias or systematic underestimation of LVEF values by the software programs could have significant clinical implications. Patients with true LVEF values above the threshold may be mistakenly excluded from potentially lifesaving treatments due to software-based underestimation. This underscores the importance of accurate and reliable LVEF measurements for informed treatment decisions and optimal patient outcomes.

Our study also demonstrated very good intra- and inter-observer reliability for LVEF determination using the four commercial software programs (ICC = 0.96–1.00; CV < 5.8 % and 6.6 %, respectively). The high reproducibility is largely attributable to the semi-automatic processing options provided by three of the programs (AN, SM, and GE-X), which minimise subjective analysis. Similar high reliability has been reported in other studies [3,10,44]. In contrast, the manual analysis required by the M-TT software led to slightly poorer intra- and inter-observer reliability. This can be ascribed to the increased subjectivity and the potential for larger random errors associated with manually delineating LV ED and -ES regions.

A limitation of this study is that the 4D-XCAT cardiac models provide only a single representation of cardiac motion. While the simulated patients encompassed a wide range of LVEF values, caution should be exercised when generalising these findings to different patient populations, especially those with left ventricular dysfunction, as the validity of such extrapolation remains uncertain. Further research is needed to explore this aspect. Additionally, most of the GBP-P studies included in the database were based on Caucasian models. This may impact the generalisability and applicability of the results to a more diverse population. However, it should be noted that the study's primary focus was on software evaluation rather than setting reference values for patients, where ethnicity would be a more critical factor.

A significant strength of this study is utilising 4D-XCAT models to simulate GBP-P studies. In contrast to many physical cardiac phantoms, these models incorporate confounding structures such as great vessels, liver, and spleen, and provide a more clinically realistic representation of cardiac and respiratory motion. The ability to compare LVEF results from the software packages to known model values enhances the accuracy of LVEF assessment in clinical practise. This will improve healthcare professionals' decision-making processes and the accuracy of their reporting.

6. Conclusion and future studies

Our study demonstrated the value of utilising an MC-simulated database of GBP-P studies to evaluate the performance of cardiac processing software in accurately determining LVEF values. This research highlights the promising accuracy of commercial software programs in determining LVEF values from simulated GBP-P studies, showcasing their potential practicality in clinical settings. We observed a strong correlation between LVEF values obtained from these software programs and the true LVEF values calculated from the LV volumes of the 4D-XCAT cardiac phantoms. This finding has significant implications for the development of new algorithms calculating LVEF from planar radionuclide ventriculography studies. Additionally, these data sets can serve as valuable tools for validating LVEF measurements, training healthcare professionals, and assessing the impact of software upgrades.

The clinical importance of accurate LVEF values and LV volumes is well-recognised, particularly for diagnosing and prognosing patients with cardiac diseases. Our study lays a foundation for future research endeavours.

Further investigations could focus on several key areas to build on this study.

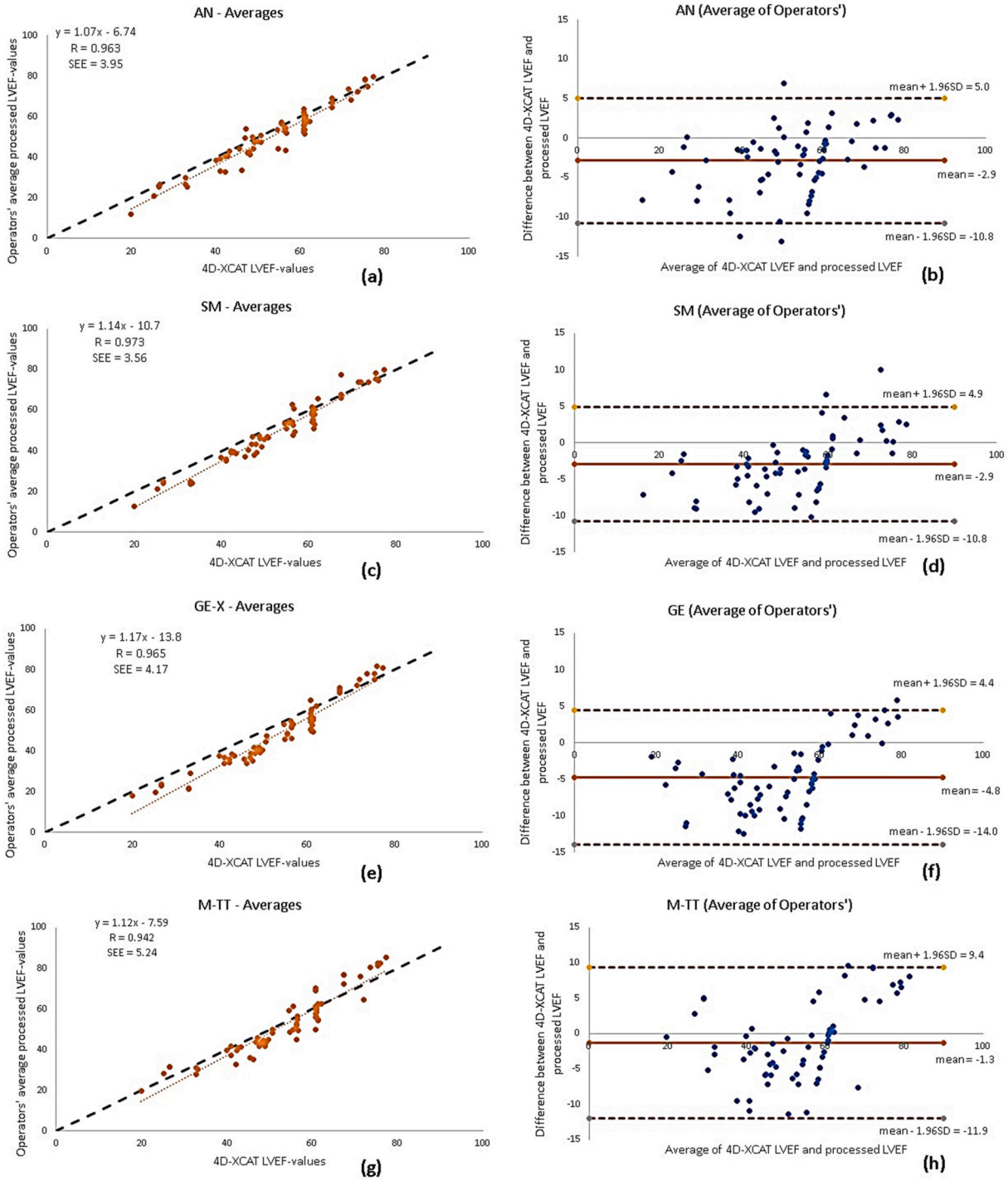

Fig. 4. Figures (a), (c), (e), and (g) present the linear regression of 4D XCAT LVEF values compared to the four processing software programs: Alfa Nuclear (AN), Siemens (SM), General Electric Xeleris (GE-X), and Mediso Tera-Tomo (M-TT). Bland-Altman analysis is shown in Figures (b), (d), (f), and (h) for the same four processing software programs: AN, SM, GE-X, and M-TT. The linear regression graphs contain the Pearson correlation coefficient (R) and the Standard Error of Estimation (SEE) for each of the software programs. The Bland-Altman graphs display a mean-, upper- and lower limit of the data.

i. Generalisability across diverse patient populations: Further research should explore the applicability of the findings to a wider range of patient populations, including those with different ethnic backgrounds and varying degrees of LV dysfunction. This will enhance the reliability and applicability of the generated database.

Table 6
Intra - and Inter-observer reproducibility results for the four processing software programs (AN: Alfa Nuclear; SM: Siemens, GE-X; General Electric Xeleris; M-TT: Mediso Tera-Tomo). Interclass correlation coefficients (ICC) with a 95 % confidence interval.

		Intra-observer reproducibility			
		AN	SM	GE-X	M-TT
Operator 1	ICC	0.99	0.99	0.99	0.96
	CV	2.29	**1.14**	2.96	5.62
Operator 2	ICC	0.99	1.00	0.99	0.98
	CV	2.61	1.71	2.34	4.64
Operator 3	ICC	0.98	0.98	0.99	0.96
	CV	3.89	3.15	4.38	**5.82**
		Inter-observer reproducibility			
		AN	SM	GE-X	M-TT
All Operators	ICC	0.99	0.96	0.99	0.97
	CV	**3.17**	4.64	4.82	**6.59**

ii. Mitigating underestimation biases: Addressing the slight underestimation of LVEF values observed at lower LVEF values could involve exploring alternative algorithms and software calibrations. Investigating advanced processing-techniques, such as machine learning algorithms, may also provide more accurate results.
iii. Expanding Modalities: Using 4D-XCAT models to simulate gated blood pool SPECT studies could extend our understanding of the accuracy of commercial software programs in determining both right and left ventricular EF and volume values.
iv. Clinical integration: Future studies could incorporate both simulated and real patient data to enhance the clinical applicability of the software programs. This would help validate the software's performance in clinical settings and ensure that it meets the needs of clinical practitioners.
v. Impact of clinical outcomes: Further research could investigate the impact of accurate LVEF and LV volume assessments on clinical decision-making, particularly in guiding chemotherapy treatment and optimising patient care. This could ultimately contribute to improved clinical outcomes for patients undergoing chemotherapy.

Funding

This work was funded by the Directorate of Research Development, University of the Free State, Bloemfontein, South Africa.

Data availability

Data will be made available on request.

CRediT authorship contribution statement

H. Pieters: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **J.A. van Staden:** Writing – review & editing, Supervision, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **H. du Raan:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation. **M.G. Nel:** Validation, Formal analysis. **G.H.J. Engelbrecht:** Validation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors acknowledge Mr Albert van Eck from the Division of High-Performance Computing at the University of the Free State, Bloemfontein, for using the high-performance cluster and his technical support. Acknowledgement also goes out to Ms. L Coetzer and Ms. I Sealanyane (Department of Nuclear Medicine Klerksdorp/Tshepong Hospital Complex) for their time and assistance in processing the data.

References

[1] C. Valzania, A. Paccagnella, A. Spadotto, I. Ruotolo, R. Bonfiglioli, F. Fallani, S. Fanti, N. Galié, Early detection of cancer therapy cardiotoxicity by radionuclide angiography: an update, J. Nucl. Cardiol. (2023), https://doi.org/10.1007/s12350-023-03202-w.

[2] G.K. Das, N.G. Chen Siew, M.A. Manap, Left ventricular ejection fraction by multigated acquisition scan using planar sodium iodide and cadmium-zinc-telluride cameras: a comparison with two-dimensional echocardiography, Asia Oceania Journal of Nuclear Medicine and Biology 11 (2023) 55–70, https://doi.org/10.22038/AOJNMB.2022.60392.1424.

[3] E.A. Bailey, D.L. Bailey, Results from an Australian and New Zealand audit of left ventricular ejection fraction from gated heart pool scan analysis, Nucl. Med. Commun. 33 (2012) 102–111, https://doi.org/10.1097/MNM.0b013e32834c2f0b.

[4] C. Sachpekidis, V. Sachpekidis, E. Moralidis, G. Arsos, Equilibrium radionuclide ventriculography: still a clinically useful method for the assessment of cardiac function? Hellenic J. Nucl. Med. 21 (2018) 213–220.

[5] T.A. Foley, S. V Mankad, N.S. Anavekar, C.R. Bonnichsen, M.F. Morris, T.D. Miller, P.A. Araoz, P. Araoz, Measuring left ventricular ejection fraction-techniques and potential pitfalls, Citation: European Cardiology 8 (2012) 108–122, https://doi.org/10.15420/ecr.2012.8.2.108.

[6] T.H. Marwick, Ejection fraction pros and cons: JACC state-of-the-art review, J. Am. Coll. Cardiol. 72 (2018) 2360–2379, https://doi.org/10.1016/j.jacc.2018.08.2162.

[7] H. Huang, P.S. Nijjar, J.R. Misialek, A. Blaes, N.P. Derrico, F. Kazmirczak, I. Klem, A. Farzaneh-Far, C. Shenoy, Accuracy of left ventricular ejection fraction by contemporary multiple gated acquisition scanning in patients with cancer: comparison with cardiovascular magnetic resonance, J. Cardiovasc. Magn. Reson. 19 (2017) 1–9, https://doi.org/10.1186/s12968-017-0348-4.

[8] R. Giubbini, E. Milan, The time for radionuclide ventriculography resurrection is coming, J. Nucl. Cardiol. 23 (2016) 1139–1141, https://doi.org/10.1007/s12350-015-0245-x.

[9] B. Hesse, T.B. Lindhardt, W. Acampa, C. Anagnostopoulos, J. Ballinger, J.J. Bax, L. Edenbrandt, A. Flotats, G. Germano, T. Gmeiner Stopar, P. Franken, A. Kelion, A. Kjaer, D. Le Guludec, M. Ljungberg, A.F. Maenhout, C. Marcassa, J. Marving, F. McKiddie, W.M. Schaefer, L. Stegger, R. Underwood, EANM/ESC guidelines for radionuclide imaging of cardiac function, Eur. J. Nucl. Med. Mol. Imag. 35 (2008) 851–885, https://doi.org/10.1007/s00259-007-0694-9.

[10] P. Bresser, J. de Beer, Y. de Wet, A study investigating variability of left ventricular ejection fraction using manual and automatic processing modes in a single setting, Radiography (2015), https://doi.org/10.1016/j.radi.2014.10.002.

[11] J.R. Fair, P.H. Heintz, R.J. Telepak, Evaluation of new data processing algorithms for planar gated ventriculography (MUGA), J. Appl. Clin. Med. Phys. 10 (2009) 173–179, https://doi.org/10.1120/jacmp.v10i3.2977.

[12] D. Mitra, S. Basu, Equilibrium radionuclide angiocardiography: its usefulness in current practice and potential future applications, World J. Radiol. 4 (2012) 421–430, https://doi.org/10.4329/wjr.v4.i10.421.

[13] H. Pieters, J.A. Van Staden, F.C.P. Du Plessis, H. Du Raan, Validation of a Monte Carlo simulated cardiac phantom for planar and SPECT studies, Phys. Med. 111 (2023), https://doi.org/10.1016/j.ejmp.2023.102617.

[14] S.C. Hiscock, M.J. Evans, R.J. Morton, D.O. Hall, Investigation of normal ranges for left ventricular ejection fraction in cardiac gated blood pool imaging studies using different processing workstations, Nucl. Med. Commun. 29 (2008) 103–109, https://doi.org/10.1097/MNM.0b013e3282f20e45.

[15] P. De Bondt, Evaluation of Cardiac Volumes by New Scintigraphic Techniques, Doctoral Thesis, University of Ghent, 2005.

[16] R. Steyn, J. Boniaszczuk, T. Geldenhuys, Comparison of estimates of left ventricular ejection fraction obtained from gated blood pool imaging, different software packages and cameras, Cardiovascular Journal of Africa 25 (2014) 44–49, https://doi.org/10.5830/CVJA-2013-082.

[17] S.N. Yang, S.S. Sun, G. Zhang, K.T. Chou, S.W. Lo, Y.R. Chiou, F.J. Li, T.C. Huang, Left ventricular ejection fraction estimation using mutual information on technetium-99m multiple-gated SPECT scans, Biomed. Eng. Online 14 (2015) 119, https://doi.org/10.1186/s12938-015-0117-2.

[18] T.R. Simon, B.S. Walker, S. Matthiesen, C. Miller, J, Triebel, J.E. Dowdey, T.C. Smitherman, A realistic dynamic cardiac phantom for evaluating radionuclide ventriculography: description and initial studies with the left ventricular chamber, The Journal of Nuclear Medicine 30 (1989) 542–547.

[19] W.P. Segars, G. Sturgeon, S. Mendonca, J. Grimes, B.M.W. Tsui, 4D XCAT phantom for multimodality imaging research, Med. Phys. 37 (2010) 4902–4915, https://doi.org/10.1118/1.3480985.

[20] W.P. Segars, M. Mahesh, T.J. Beck, E.C. Frey, B.M.W. Tsui, Realistic CT simulation using the 4D XCAT phantom, Med. Phys. 35 (2008) 3800–3808, https://doi.org/10.1118/1.2955743.

[21] W.P. Segars, B.M.W. Tsui, J. Cai, F.-F. Yin, G.S.K. Fung, E. Samei, Application of the 4D XCAT phantoms in biomedical imaging and beyond, IEEE Trans. Med. Imag. 37 (2018) 680–692, https://doi.org/10.1109/TMI.2017.2738448.

[22] W.P. Segars, J. Bond, J. Frush, S. Hon, C. Eckersley, C.H. Williams, J. Feng, D.J. Tward, J.T. Ratnanather, M.I. Miller, D. Frush, E. Samei, Population of anatomically variable 4D XCAT adult phantoms for imaging research and optimization, Med. Phys. 40 (2013), https://doi.org/10.1118/1.4794178.

[23] W.P. Segars, A.I. Veress, G.M. Sturgeon, E. Samei, Incorporation of the living heart model into the 4D XCAT phantom for cardiac imaging research, IEEE Transactions on Radiation and Plasma Medical Sciences 3 (2019) 54–60, https://doi.org/10.1109/TRPMS.2018.2823060.

[24] M. Ljungberg, The SIMIND Monte Carlo program, Sweden, Version 6.2, 2020. https://www.msf.lu.se/research/simind-monte-carlo-program/downloads.

[25] N. Kawel-Boehm, S.J. Hetzel, B. Ambale-Venkatesh, G. Captur, C.J. Francois, M. Jerosch-Herold, M. Salerno, S.D. Teague, E. Valsangiacomo-Buechel, R.J. van der Geest, D.A. Bluemke, Reference ranges ("normal values") for cardiovascular magnetic resonance (CMR) in adults and children: 2020 update, J. Cardiovasc. Magn. Reson. 22 (2020), https://doi.org/10.1186/s12968-020-00683-3.

[26] M.B. Farrell, J.R. Galt, P. Georgoulias, S. Malhotra, R. Pagnanelli, C. Rischpler, B. Savir-Baruch, SNMMI procedure standard/EANM guideline for gated equilibrium radionuclide angiography, J. Nucl. Med. Technol. 48 (2020) 126–135, https://doi.org/10.2967/jnmt.120.246405.

[27] A. Nicol, M. Avison, M. Harbinson, S. Jeans, W. Waddington, S. Woldman, Procedure guideline for planar radionuclide cardiac ventriculogram for the assessment of left ventricular systolic function, Nucl. Med. Commun. 2 (2016), https://doi.org/10.1097/MNM.0b013e328321cdba.

[28] M. Ljungberg, Monte Carlo simulations for therapy imaging, J. Phys. Conf. 317 (2011), https://doi.org/10.1088/1742-6596/317/1/012016.

[29] C.A. Schneider, W.S. Rasband, K.W. Eliceiri, NIH image to ImageJ: 25 years of image analysis HHS public access, Nat. Methods 9 (2012) 671–675, 10.1038/nmeth.2089.

[30] K.V. Bunting, R.P. Steeds, L.T. Slater, J.K. Rogers, G.V. Gkoutos, D. Kotecha, A practical guide to assess the reproducibility of echocardiographic measurements, J. Am. Soc. Echocardiogr. 32 (2019) 1505–1515, https://doi.org/10.1016/j.echo.2019.08.015.

[31] IM512P , (n.d.). http://alfanuclear.com/SitioAlfa_3/EnglishSite/IM/IM512P.htm (accessed August 15, 2023).

[32] Siemens Healthineers, syngo.via - Siemens Healthineers , (n.d.). https://www.siemens-healthineers.com/medical-imaging-it/advanced-visualization-solutions/syngovia (accessed August 15, 2023).

[33] Xeleris WS 2.0 | GE HealthCare Service Shop USA , (n.d.). https://services.gehealthcare.com/gehcstorefront/c/DI_CTG_L2_NM_09 (accessed August 15, 2023).

[34] Mediso - InterView^{TM} FUSION processing software , (n.d.). https://mediso.com/global/en/product/interview-processing-workstation/interview-fusion-processing-software (accessed August 15, 2023).

[35] Laerd statistics, One-way ANOVA - an introduction to when you should run this test and the test hypothesis, Laerd Statistics (2018). https://statistics.laerd.com/statistical-guides/one-way-anova-statistical-guide.php.

[36] D. Giavarina, Understanding Bland altman analysis, Biochem. Med. 25 (2015) 141–151, https://doi.org/10.11613/BM.2015.015.

[37] Y.H. Chan, Biostatistics 104: correlational analysis, Singapore Medical Journal 44 (2003) 614–619.

[38] Zach, What is the standard error of the estimate? (Definition & example). https://www.statology.org/standard-error-of-estimate/, 2021. (Accessed 9 September 2023).

[39] Microsoft support, use the analysis ToolPak to perform complex data analysis - microsoft support. https://support.microsoft.com/en-us/office/use-the-analysis-toolpak-to-perform-complex-data-analysis-6c67ccf0-f4a9-487c-8dec-bdb5a2cefab6, 2024.

[40] T.K. Koo, M.Y. Li, A guideline of selecting and reporting intraclass correlation coefficients for reliability research, Journal of Chiropractic Medicine 15 (2016) 155–163, https://doi.org/10.1016/j.jcm.2016.02.012.

[41] Free Download | Real Statistics Using Excel , (n.d.). https://real-statistics.com/free-download/(accessed August 15, 2023).

[42] J.R. Landis, G.G. Koch, The measurement of observer agreement for categorical data, Source: Biometrics 33 (1977) 159–174.
[43] A. Krakovich, U. Zaretsky, E. Gelbart, I. Moalem, A. Naimushin, E. Rozen, M. Scheinowitz, R. Goldkorn, Anthropomorphic cardiac phantom for dynamic SPECT, J. Nucl. Cardiol. 30 (2023) 516–527, https://doi.org/10.1007/s12350-022-03024-2.
[44] J. V Skrypniuk, D. Bailey, P.S. Cosgriff, J.S. Fleming, A.S. Houston, P.H. Jarritt, D.R. Whalley, UK Audit of Left Ventricular Ejection Fraction Estimation from Equilibrium ECG Gated Blood Pool Images, Lippincott Williams & Wilkins, 2005.