




Research Article

Accuracy and Precision of Bone Scan, Magnetic Resonance Imaging (MRI) and Digital Radiography in Limb Salvage Surgery for Long Bone Tumors

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Received: 19 December 2022; **Revised:** 8 March 2023; **Accepted:** 6 April 2023

Abstract: Introduction: The aim of this study is to evaluate the level of accuracy and precision of bone scan (BS), magnetic resonance imaging (MRI) and digital radiography (DR) to measure long bone tumors to design custom made prosthesis (CMP)/modular prosthesis (MP) in limb salvage surgery (LSS). **Material and methods:** There are two separate groups, one is phantom study and another one is patient's study. *Phantom study:* done with Jaszack phantom for gamma camera (GC) and indigenous phantom for MRI and DR. Three independent imaging professionals (nuclear medicine physicians and radiologists) measured the distance between standardized, preselected points on the Jaszack phantom in the GC and indigenous phantom on the coronal and sagittal view of the MRI scan and in DR. The measured values were compared it with the known values for phantom measurement. *Patient's study:* Patients with a malignant bone tumor of the lower/upper limbs enrolled from 2020-2021 at the institute were taken up for the retrospective study. Totally 36 patients were enrolled, 24 patients were male (Ages: 2 to 45 years) and 12 patients were female (Ages: 8 to 18 years). Three independent imaging professionals measured the patient's long bone in the BS, MRI and DR and compared with histopathological specimen measurement after LSS. **Statistical analysis:** Descriptive statistics using appropriate measures of central tendency, dispersion, Karl-Pearson correlation coefficient and paired t-test were employed. **Results:** A near perfect positive correlation was evident between all three pairs of the BS, MRI scan and DR values and a positive agreement within 1 mm was around 95%. **Conclusion:** For the phantom study, we conclude that GC and MRI measurements are equal in physical measurements and multiplication correction factor (MCF) = 1. DR measurements were found to be near equal physical measurements and MCF = 0.9104 and three observer's measurements values were also near normal.

Keywords: multiplication correction factor, bone scan, magnetic resonance imaging, digital radiography, custom-made prosthesis, limb salvage surgery

1. Introduction

Our goal of tumor surgery is complete resection of disease via wide excision and surgical options can be divided into amputation and limb salvage surgery (LSS) [1]. In 1943, Austin Moore developed the first endoprosthesis fashioned from Vitallium, providing the first alternative to traditional amputation as the primary treatment of bone tumors and it was used for the first metallic endoprosthesis in orthopedic oncology [2]. Recent advances in imaging technology and the use of bone scan (BS), magnetic resonance imaging (MRI) scan and digital radiography (DR) in musculoskeletal oncology for the measurement of long bone lesions are helpful in designing prostheses for LSS. Plain radiography, computed tomography (CT) scan, MRI scan, and bone scintigraphy can help to diagnose and staging of bone tumors [3]. Measurement of the long bone lesion should be accurate for designing prosthesis, for which we have developed indigenous phantom for MRI and DR. Quality control was done using Jaszack phantom for gamma camera (GC) to evaluate the accuracy of long bone tumor measurements.

The aim of this study is to evaluate the level of accuracy and precision of long bone tumor measurement of BS, MRI and DR. The study also includes the repeatability and reproducibility of tumor measurement to design custom-made prosthesis (CMP)/modular prosthesis (MP) in LSS for osteosarcoma (OS) and Ewing's sarcoma (ES) patients with the help of phantoms and patients' study

2. Materials and methods

The first study was done using Jaszack phantom for GC and indigenous phantom (Figure 1) for MRI and DR. Three observers measured the distance between standardized, preselected points on the Jaszack phantom in the GC. Using indigenous phantom on the coronal and sagittal views of the MRI scan and in DR the measurements were recorded. The measured values were compared with the known values for phantom measurement by three independent imaging professionals (nuclear medicine physicians and radiologists) to check the accuracy, precision, repeatability and reproducibility.

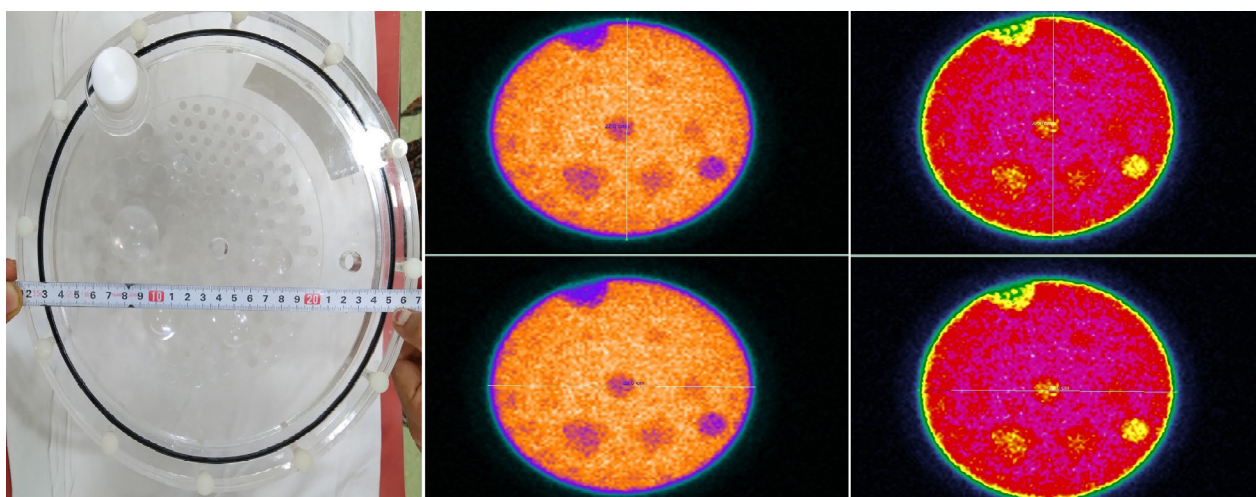


Figure 1. Measurements in Jaszack phantom - GC

The next study was carried out involving 36 patients, which includes 24 males and 12 females. Three individual imaging professionals measured long bone lesion in the BS, MRI and DR. The measured values were also compared with histopathological specimen measurement and after LSS. Patients with malignant bone tumor of the lower/upper limbs especially OS and ES enrolled from 2020-2022 at the institute were taken up for the study. Totally 36 patients were enrolled who satisfied the eligibility criteria for this study. Measurements were compared with histopathological

specimens' post-surgery to check accuracy, repeatability and reproducibility.

The phantom study and patient's study are relevant to this study. Phantom's study is to check the accuracy and precision and patient's study is to check the repeatability and reproducibility.

2.1 Statistical method

Descriptive statistics using appropriate measures of central tendency and dispersion were employed to describe the data. Karl-Pearson correlation coefficient was used to establish the association between continuous covariates. Paired t-test was utilized to test the differences in paired values for statistical significance.

2.2 Methodology

In the phantom study, we used a Jaszack phantom study in GC and compared the physical dimension and scintigraphic dimension in delayed static and single photon emission computed tomography (SPECT) acquisition modes.

In GC study, we used Jaszack phantom, we filled with 25 mCi of Tc99m-pertechnetate and water without air bubbles in GC. Based on our experience if we perform a phantom study immediately with 3 mCi of Tc99m pertechnetate, it will be a heterogeneous distribution with water. Uniform distribution of Tc99m pertechnetate with water after 18 to 24 hours only. For that only we are adding 20-25 mCi. After 18 hours, we performed the delayed static and SPECT scan after the completion of the acquisition, we have drawn the diameter of the phantom and took the measurements and checked with the physical measurements of the diameter of the phantom (Figure 1).

For the MRI scan, we used indigenous phantom consisting of a plastic bottle fitted with a glass rod in the center, filled with water and MRI scan was done. Processing in coronal and sagittal sections was done and the phantom length, as well as width measurements, were noted (Figure 2). The dimensions of the glass rod were measured using inbuilt tools of the application software and compared with physical measurement. In DR, the indigenous phantom was scanned without water with a film focal distance (FFD) of 100 cm, 96.5 cm and 103.5 cm and measurements of the glass rod was measured with computer-inbuilt tools and compared with physical measurements. Water has not influenced by electromagnetic radiation like x-ray, phantoms with and without water will give the same measurements (Figure 2).

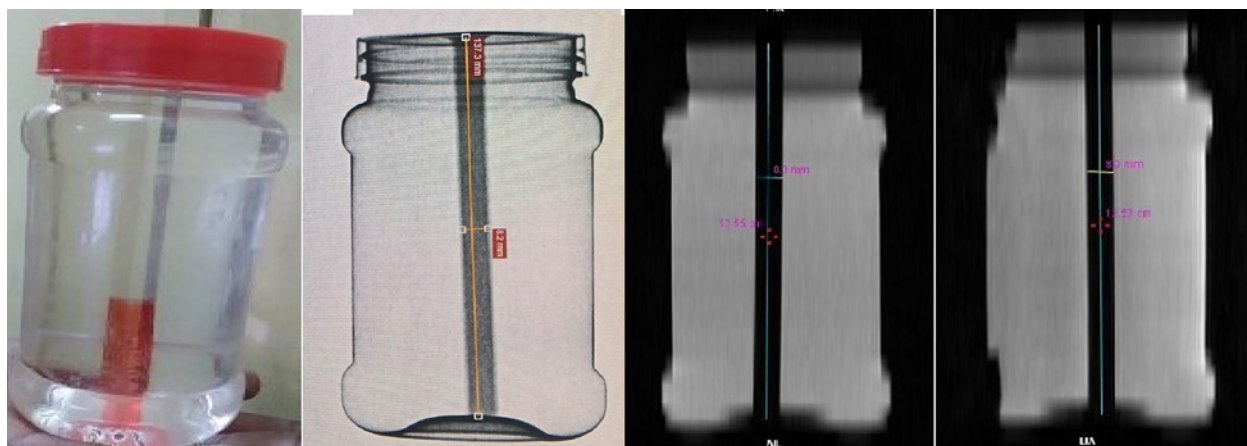


Figure 2. Measurements in indigenous phantom - DR and MRI (coronal and sagittal section)

Water will not mimic soft tissue in a real patient. But the principle of MRI scan is the hydrogen nucleus is the magnetic resonance (MR) active nucleus used in clinical MRI. It is used because it is very abundant in the human body. If we are using a phantom with water and it contains a large number of hydrogen atoms, possibility for tissue characterization and blood flow imaging. So, without a hydrogen atom (water), MRI scan is not possible to do imaging.

The magnification correction factor (MCF) was determined with the help of phantom study in GC, MRI and DR for all long bone tumors in the BS, MRI and DR. Phantom measurements were carried out by three independent imaging

professionals, and measurement is uniformly done using system inbuilt tools to study the precision, repeatability and reproducibility. The purpose of the indigenous phantom for MRI/DR is to give the measurements accurately and precisely for our study and it has been well-validated by our professionals.

For the patient's study, we used Tc99m, methylene diphosphonate (MDP) BS SPECT, MRI scan and DR for each patient with informed consent. From a quantification point of view, the patient's original height in centimeters was compared with whole body profile image height. It has been found that both are well correlated [4]. This is done for all patients and is documented. Long bone measurements were done by three independent imaging professionals in the BS, MRI and DR (Figures 3 and 4).

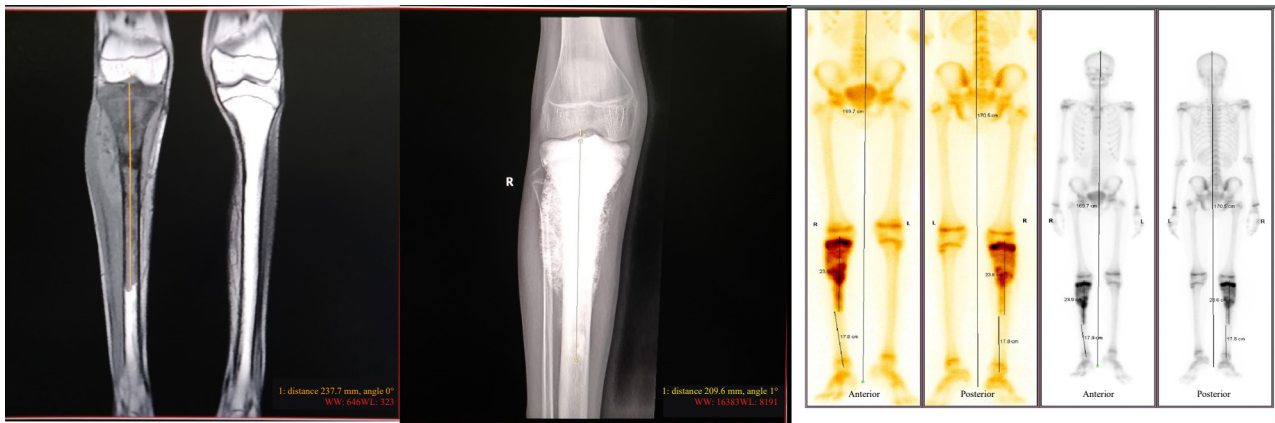


Figure 3. Tumor measurement in tibia - MRI, DR and BS



Figure 4. Tumor measurement in femur - MRI, DR and BS

2.3 Technique

The BS was done after injecting 20 mCi of Tc99m MDP intravenously into the patient. After good hydration and frequent emptying of the bladder, static images were acquired after 3 hours. Whole body images were acquired with anterior and posterior views and SPECT images were also acquired. After processing, the images were displayed in dual intensity format, one for the axial skeleton and another for the appendicular skeleton. For measurement purposes, we used zooming option for the one pair of images. Zoom factor was 2.0 and color code (color scale) was REV HOTIRON. Another set of images in black and white (grayscale) was used with zoom factor of 1.0. The cranio-caudal (CC) extension of the tumor from upper to lower end was measured from BS anterior and posterior views of the whole-body BS. Also, we measured the uninvolved bone length and recorded it [4]. The protocol used in GE Infinia Dual Head GC/GE Discovery 630 Dual Head GC for BS- SPECT (Table 1), static scan (Table 2) and whole body BS (Table 3) are explained.

Table 1. BS and Jaszack phantom SPECT - protocol

Technical parameters	Detector-1	Detector-2
Detector settings	Anterior	Posterior
Scan location		H mode
Start angle		0 degree
Body contour		Yes
Scan mode		Step and shoot
Stop on time per projection		40 sec
Matrix		128 x 128
Energy session		
Isotope		Tc99m
Energy range		Low energy
Field engineer (FE) mode: Normal - routine scans; Fast - SPECT studies		Normal
Energy map name		Tc99m map
Collimator		Low energy high resolution (LEHR)
Center of rotation (COR) correction		Yes
Uniformity map		Tc99m LEHR
Window peak	-%	+
140 KeV	-10%	+10%
Table height		74.95 cm on fixed pallet support
Rotation		
Total angular per range		360 degree
Arc per detector		180 degree
View per angle		6 degree
Number of views		60
Direction		Clockwise (CW)
Repeat		1 time
Field of View (FOV) settings		
Number of FOV's		1
FOV time multiplier		1
Rough overlap		4 degree
Direction		Table IN
Range		40 cm

Table 2. BS and Jaszack phantom static - protocol

Technical parameters	Detector-1	Detector-2
Detector settings	Anterior	Posterior
Scan location		H mode
Start angle		0 degree
Scan speed		10 cm/minute
Body contour		Yes
Matrix		256 x 256
Energy session		
Isotope		Tc99m
Energy range		Low energy
FE mode		Normal
Energy map name		Tc99m map
Collimator		LEHR
COR correction		Yes
Uniformity map		Tc99m LEHR
Window peak	-%	+
140 KeV	-10%	+10%
Table height		74.95 cm on fixed pallet support
FOV settings		
Number of FOV's		1
FOV time multiplier		1
Direction		Table IN
Range		40 cm

Table 3. Whole body BS - protocol

Technical parameters	Detector-1	Detector-2
Detector settings	Anterior	Posterior
Scan location		H mode
Body contour		Yes
Detector length		195 cm
Scan mode		Continuous
Scan speed		8 cm/minute
Matrix		1024 x 256
Energy session		
Isotope		Tc99m
Energy range		Low energy
Energy map name		Tc99m map
Collimator		LEHR
Scan mode		Continuous
Scan speed		8 cm/minute
Uniformity map		Tc99m LEHR
Window peak	-%	+
140 KeV	-10%	+10%
Table height	74.95 cm on fixed pallet support	

MRI scan was done for long bone (ie) CC, medio-lateral (ML) and antero-posterior (AP) of the tumor dimension and the marrow involvement was also studied. The three-dimensional measurement of long bone was done by radiologist using computer system in-built tools [4]. The protocol is explained in Table 4.

Table 4. MRI sequences for long bones and indigenous phantom - protocol

	MRI
Plain	Axial T1, T2 and Short tau inversion recovery (STIR); Coronal T1, T2 and STIR Sagittal STIR Diffusion-weighted image axial Apparent diffusion coefficient axial Proton density image with fat suppression (coronal, sagittal and axial plane) Axial gradient echo
Precontrast sequences	Axial T1 with fat suppression
Postcontrast sequences	Axial T1 with fat suppression Coronal T1 with fat suppression Sagittal T1 with fat suppression

DR of long bone was done to measure the tumor size especially CC measurement in pre and post-neoadjuvant chemotherapy (NAC). The CC measurement of long bone is done by radiologist using computer in-built tools. The protocol is explained in detail in Table 3. Long bone measurement was done by three independent imaging professionals using system inbuilt tools to study accuracy, precision, repeatability and reproducibility. Acquisition protocols are in Table 5.

Table 5. DR for phantom and long bone (femur, tibia, humerus, etc.) - protocols

DR			
FOV	Include entire length of bone with any one joint		
Views	AP and lateral views		
Source to image distance	100 cm		
Grid	Yes		
Landmark	Femur	Tibia	Humerus
	Mid-thigh	Mid-leg	Mid-arm
mA	150 - 200	150 - 200	150 - 200
Kvp	60 - 80	55 - 75	50 - 70
mAs	20 - 40	15 - 35	10 - 30
Cassette	14 x 17 inches		

3. Results

3.1 Study-1 (Phantom study)

In the phantom study (Figure 5), we have standardized the MCF with the help of phantom study in GC magnification factor (MF) = 1.0 (Table 6), and MRI MF = 1.0 (Table 7).

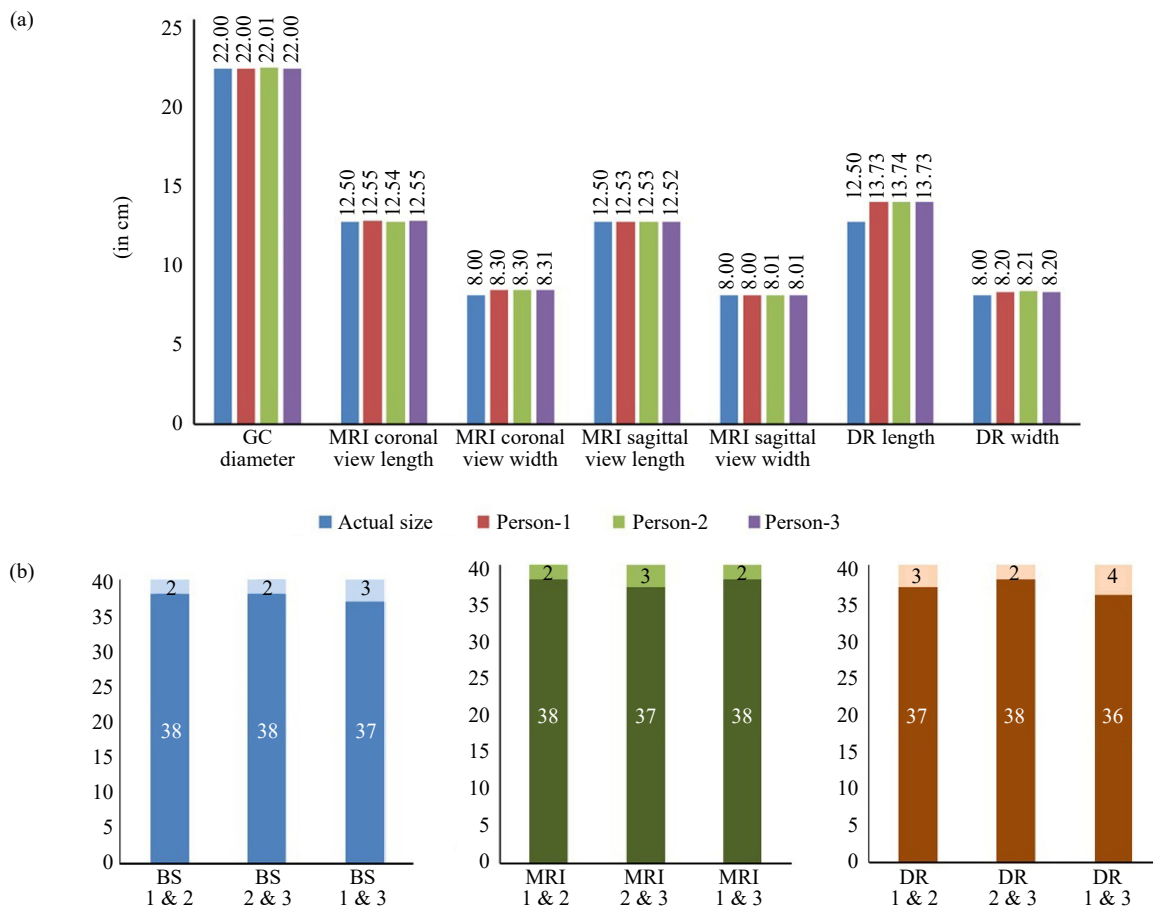


Figure 5. (a) Phantom's study for 3 imaging professionals using GC, MRI and DR; (b) 1% agreement among 3 imaging professionals in BS, MRI and DR

Table 6. Jaszack phantom dimension in GC (GE Discovery 630 and Infinia Dual GC)

Jaszack phantom dimension	
Physical measurement (diameter of phantom)	22.0 cm
Scintigraphic measurement (diameter of phantom)	22.0 cm
MF	1.0

Table 7. Indigenous glass phantom in MRI scan

Indigenous-glass Phantom	Physical measurement	MRI scan coronal view	MRI scan sagittal view
Phantom length	12.5 cm	12.55 cm	12.53 cm
MF		12.5/12.55	12.5/12.53
		0.996	0.997
Phantom width	8.0 cm	8.03 cm	8.0
MF		8/8.03	8.0/8.0
		0.964	1

All DR was taken in 100 cm FFD, so DR MF = 0.9104 at FFD = 100 cm (Table 8).

Table 8. Indigenous-glass phantom in DR

Indigenous-glass phantom	Physical measurement	DR (FFD = 100 cm)	DR (FFD = 96.5 cm)	DR (FFD = 103.5 cm)
Phantom length	12.5 cm	13.73 cm	14.22 cm	14.09 cm
MF		12.5/13.73	12.5/14.22	12.5/14.09
		0.9104	0.8790	0.8872
Phantom width	8.0 cm	8.2 cm	8.4 cm	8.6 cm
MF		8/8.2	8/8.4	8/8.6
		0.9756	0.9524	0.9303

3.2 Study-2 (Patient's study)

Measures of central tendency and deviation were used to describe the sample characteristics. Student's paired t-test was employed to test for statistical significance of the mean differences of different parametric paired values observed by three persons. Pearson's correlation coefficient was utilized to establish the association between the paired values.

The difference in the mean values of the paired differences with respect to BS values was statistically not significant between Person 1 and Person 2 ($p = 0.585$) as well as Person 2 and Person 3 ($p = 0.333$). A positive agreement within 1 mm of BS values was forthcoming in 95% of both pairs. The agreement status was 92.5% between Person 1 and Person 3 and mean differences were statistically significant ($p < 0.001$). A near perfect positive correlation was evident between all three pairs ($p < 0.001$) of BS values (Table 9).

Table 9. Correlation, paired differences and agreement status on BS values between three professionals

BS	Person 1 vs Person 2	Person 1 vs Person 3	Person 2 vs Person 3
Number (N)	40	40	40
Mean scores	12.1545 SD ± 4.44653	12.1545 SD ± 4.44653	12.1487 SD ± 4.46345
	12.1487 SD ± 4.46345	12.1589 SD ± 4.44734	12.1589 SD ± 4.44734
Paired mean difference	0.00575 SD ± 0.06611	0.00437 SD ± 0.00590	0.01012 SD ± 0.06531
p-value	0.585	< 0.001	0.333
Agreement ≤ 1 mm	95%	92.5%	95%
Correlation coefficient	1.00	1.00	1.00
p-value	< 0.001	< 0.001	< 0.001

A positive agreement within 1 mm of MRI scan of every paired value between the three persons ranged between 92.5% and 95%. The difference in the mean values of the paired differences with respect to MRI scan values was statistically not significant between Person 1 and Person 3 ($p = 0.089$) as well as Person 2 and Person 3 ($p = 0.483$). A near perfect positive correlation was evident between all three pairs of MRI scan values (Table 10).

Table 10. Correlation, paired differences and agreement status on MRI scan values between three professionals

MRI scan	Person 1 vs Person 2	Person 1 vs Person 3	Person 2 vs Person 3
N	40	40	40
Mean scores	12.2200 SD ± 4.50847	12.2200 SD ± 4.50847	12.2252 SD ± 4.50998
	12.2252 SD ± 4.50998	12.2287 SD ± 4.50830	12.2287 SD ± 4.50830
Paired mean difference	0.00525 ± SD ± 0.00784	0.00875 SD ± 0.03174	0.01012 SD ± 0.06531
p-value	0.585	< 0.001	0.333
Agreement ≤ 1 mm	95%	92.5%	95%
Correlation coefficient	1.00	1.00	1.00
p-value	< 0.001	< 0.001	< 0.001

A near perfect positive correlation was evident between all three pairs of digital radiology scan values ($p \leq 0.001$). A positive agreement within 1 mm of digital radiology scan values was 90% between Person 1 and Person 3, 92.5% for Person 1 and Person 2 and 95% between Person 2 and Person 3. The difference in the mean values of the paired differences with respect to digital radiology scan values was statistically not significant between Person 2 and Person 3 ($p = 0.139$) but statistically significant ($p = 0.007$) for the other two pairs (Table 11).

Table 11. Correlation, paired differences and agreement status on DR scan values between three professionals

DR	Person 1 vs Person 2	Person 1 vs Person 3	Person 2 vs Person 3
N	40	40	40
Mean scores	11.4660 SD \pm 4.43434	11.4660 SD \pm 4.43434	11.4735 SD \pm 4.44198
	11.4735 SD \pm 4.44198	11.4696 SD \pm 4.43436	11.4696 SD \pm 4.43436
Paired mean difference	0.00750 SD \pm 0.01679	0.00362 SD \pm 0.00801	0.00388 SD \pm 0.01623
p-value	0.007	0.007	0.139
Agreement \leq 1 mm	92.5%	90%	95%
Correlation coefficient	1.00	1.00	1.00
p-value	< 0.001	< 0.001	< 0.001

4. Discussion

The measurement of a relatively small length (1 mm) on BS. MRI and digital radiographs have gained increasing importance regarding outcomes and indications in orthopedic surgery like LSS to design prostheses [5]. The results of this study are applicable under ideal conditions and in vivo measurements most likely would be more accurate because three different three independent imaging professionals (nuclear medicine physician) in the BS and (radiologists) in MRI scan and DR carried out the measurement to give the appropriate length of the long bone tumor. The reliability, reproducibility, accuracy and precision of the measurements were analyzed. This highlights the importance of comparing the measurements of multiple observers before making conclusions. As expected, measurements were much closer to the known values.

5. Conclusion

From the phantom study results we can conclude that GC and MRI measurements are comparable to physical measurements MCF = 1. DR measurements MF = 0.9104 at FFD = 100 cm were found. Three observers' measurement values are also close to the actual value. The results of the patient's study indicate that BS, MRI and DR measurements of three independent imaging professionals are also close to pathological specimen measurements done by pathologists after LSS. With three independent imaging professionals' reliability, repeatability, reproducibility and accuracy were ensured in tumor length measurements for designing CMP or MP for patients who are affected by OS and ES. In view of doing prosthesis, to find out whether Tc99m MDP BS is an alternative method for MRI scan or not.

Acknowledgements

This study was done as a prelude to the Ph.D. work at Tamil Nadu Dr. M.G.R. Medical University.

Ethical consent

The authors have obtained the institute's ethical committee clearance for this study. Reference No: IEC/2022/May 03 dated 25/05/2022 and trials were approved by our statistician (i.e., 36 patients only).

Conflict of interest

The authors declare no competing interests.

References

- [1] Misaghi A, Goldin A, Awad M, Kulidjian AA. Osteosarcoma: a comprehensive review. *SICOT-J*. 2018; 4: 12. <https://doi.org/10.1051/sicotj/2017028>
- [2] Hwang JS, Mehta AD, Yoon RS, Beebe KS. From amputation to limb salvage reconstruction: Evolution and role of the endoprosthesis in musculoskeletal oncology. *Journal of Orthopaedics and Traumatology*. 2014; 15: 81-86. <https://doi.org/10.1007/s10195-013-0265-8>
- [3] Iwanowska B, Brągoszewska H, Mądzik J, Szkudlińska-Pawlak S, Kopyś-Wiszniewska I, Jastrzębska M, et al. Imaging of complications after limb prostheses implantation in children with bone tumors. *Polish Journal of Radiology*. 2017; 82: 227-232. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5411374/>
- [4] Rangarajan GK, Krishnakumar R, Raja A, Singh SS, Manivannan N. Role of bone scan and MRI in designing of customized prosthesis for limb salvage surgery of long bone tumors: 4 years of single institution analysis. *Indian Journal of Surgical Oncology*. 2022; 13: 364-371. <https://doi.org/10.1007/s13193-021-01475-6>
- [5] Fowler JR, Ilyas AM. The accuracy of digital radiography in orthopaedic applications. *Clinical Orthopaedics and Related Research*. 2011; 469(6): 1781-1784. <https://doi.org/10.1007/s11999-010-1628-6>