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Assessment of a three-dimensional measurement technique for the porosity evaluation of PMMA bone cement

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Abstract *In vitro* testing of bone cement has historically resulted in the belief that porosity should be minimised to help reduce the risk of prosthesis failure through aseptic loosening. Traditional porosity measurement techniques rely on the analysis of a two dimensional representation of a three dimensional structure. However, with an increasing interest in the number, size and distribution of pores in bone cement, the reliability of a two dimensional approach is questionable. The purpose of this study was to investigate the use of micro computed tomography (micro-CT) for the three dimensional measurement of bone cement porosity by comparison with two traditional techniques. Eighteen bone cement specimens were analysed for porosity using each technique. Levels of agreement between techniques were evaluated, and technique precision was assessed in terms of repeatability and sensitivity to changes in threshold. Micro-CT data was used to illustrate the effectiveness of predicting the porosity of a whole structure from a sample region; an approach often used with traditional techniques. In summary, poor agreement was found between all techniques. However, micro-CT was found to be significantly more repeatable and less sensitive to changes in threshold. The results demonstrated that porosity cannot be reliably determined using traditional techniques and that a large proportion of a specimen is required to provide an accurate porosity measurement.

1. Introduction

Polymethylmethacrylate (PMMA) bone cement is widely used in orthopaedics as a means of fixation in total joint replacement surgery. The majority of failures occur as a result of aseptic loosening, a multifactorial phenomenon, to which a contributory factor may be mechanical failure of the cement mantle, the cement-prosthesis interface, or the cement-bone interface [1]. One widely accepted approach to alleviate the risk of loosening due to cement failure is to reduce porosity. It has been demonstrated that a reduction in the porosity of bone cement improves compressive [2–4] and flexural properties [2, 5, 6] and extends fatigue life [7–9] in a laboratory environment. Conversely, porosity reduction has been shown to increase cement shrinkage, which may be detrimental to the cement-bone or cement-prosthesis interface [10, 11]. A number of factors that affect the bulk porosity of bone cement have been previously explored. The efficacy of techniques such as vacuum mixing [2, 4, 8, 9, 11–13] and centrifugation [7, 12–15] in reducing porosity have been investigated. In addition, pre-chilling of cement constituents [4, 7, 9, 15, 16] and changes in cement formulations [4, 15] have been shown to influence porosity. Porosity measurement has also been used as an indicator of preparer technique and variability [12, 17].

Traditionally, two main approaches to the *in vitro* determination of bone cement porosity have been adopted. These involve using either high-resolution radiography [2, 4, 6, 7, 12, 16, 17] or light microscopy [3–5, 7–9, 11, 15–18] to provide a two dimensional (2D) representation of porosity. A potential problem with using a 2D measurement is that it relies on the cement having a relatively homogeneous pore distribution.

The current consensus remains that techniques should be adopted to reduce the number and size of pores created during mixing. However, a large variation in the fatigue strength of cements mixed under reduced pressure has been reported and is thought to be due to different porosity distributions [8]. Researchers are therefore becoming increasingly

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interested in the number, size and distribution of pores rather than merely the area porosity. It is difficult to adequately predict the relationship between porosity and fatigue strength through *in vitro* testing. *In vivo*, it is unlikely that the cement mantle will be under homogenous stress, which may result in pores in localised areas initiating cracks [19]. In fact, it may be the case that pores actually prolong implant life through blunting propagating cracks [20]. There is also the potential problem associated with cement shrinkage, where in constrained cases, pores may be induced at the cement-bone or cement-stem interface [10]. In the recent paper by Macaulay *et al*. [12] a call is made for further studies to correlate fatigue with porosity and hence determine an optimal porosity reduction technique. They further suggest that traditional porosity measurement techniques, which involve the analysis of a 2D representation of a three dimensional (3D) object, could be improved by the image analysis of multiple axial sections.

Micro computed tomography (micro-CT) can provide a powerful non-destructive 3D approach to quantifying the porosity of materials, however, it does not appear that any previous publications have described this technique for the measurement of bone cement. The aim of this study is to compare traditional 2D techniques for bone cement porosity measurement with a new three-dimensional method using micro-CT.

2. Methods

Eighteen cylindrical specimens (6 mm diameter, 12 mm height) were randomly selected for measurement from batches of PMMA bone cement (CMW3 and Endurance) supplied by the manufacturer (DePuy-CMW, UK). All of the specimens were scanned initially using a micro-CT scanner (μCT 80, Scanco, Switzerland) at a resolution of 20 μm. An area of interest (AOI) was scanned that had a reduced diameter to eliminate edge effects and cylinder ends were cropped as they were found to be slightly concave. A threshold intensity was selected to separate cement and pores and then kept constant through all subsequent micro-CT measurements. Using software provided by the manufacturer, a 3D reconstruction of each cylinder was performed, and then reversed in order to visualise the pore distribution as illustrated in Fig. 1. Tiff images of each CT slice were exported and analysed using custom written software (IDL, Research Systems, CO) to determine the volume of each pore and total porosity relative to the cylinder volume.

A 2 mm transverse disc was then sectioned from each specimen using a water cooled diamond cutter. Residual debris was removed using an ultrasonic cleanser and both surfaces of the discs were polished to a mirror finish.

For the measurement of bone cement porosity using radiography, a methodology was adopted based on

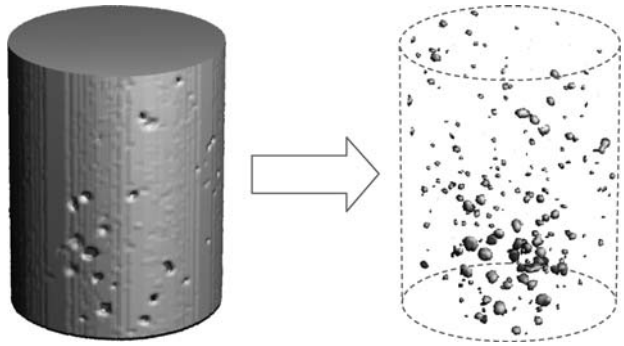

Fig. 1 Micro-CT 3D reconstruction showing pore distribution.

techniques used previously [3, 8, 15]. Each disc was radiographed 20 kV, 4 mA) using a high-resolution radiography machine built in-house at the University of Leeds. Resulting radiographs taken were digitised using an optical microscope and digital camera. A threshold intensity was determined visually by the operator to determine the pore outline. The total pore area in pixels was then calculated using image analysis software (Image-Pro Plus, Media Cybernetics, USA) and the 2D porosity determined relative to the total surface area. Each radiograph was analysed twice by the same operator.

The discs were then stained with a red dye penetrant and the surfaces examined using an optical microscope with a digital camera attached. The methodology for porosity measurement using microscopy was also based on previously used techniques [6, 12, 16]. Images of each surface were downloaded and analysed as before using Image-Pro Plus. Images of both sides of each disc were analysed twice by the same operator.

Finally, each disc was imaged using micro-CT at a resolution of 20 μm and analysed for porosity using the same method that was used for the intact cylinders. Micro-CT measurements of the discs were taken twice with a constant threshold intensity used throughout.

Repeatability of the micro-CT and radiography techniques was assessed using the standard statistical technique described by Bland and Altman [21]. This involved calculating the standard deviation in the difference between the two measurements of each disc. For microscopy, the standard deviation in the difference between the two measurements of both surfaces of each disc was calculated. In order to assess technique sensitivity, the porosity was also recalculated for one disc using each method with the threshold increased and decreased by 10% of the initial value. To evaluate how effective disc measurements were in predicting the porosity of the whole cylinders, three regions (equal to the disc dimensions) within each whole specimen micro-CT scan were also analysed for porosity. Agreement between the three porosity measurement techniques was also assessed using the techniques described by Bland and Altman [21].

Table 1 Porosity measurements of 18 specimens

	Micro-CT (discs)	Radiography	Microscopy
Mean % porosity	0.11	0.43	0.38
Standard deviation	0.09	0.43	0.54

Table 2 Summary of technique precision

	Micro-CT (discs)	Radiography	Microscopy
Standard deviation in the difference between repeated measurements	0.032	0.168	0.111
Percent change in porosity for 10% change in threshold	0.15	400	12

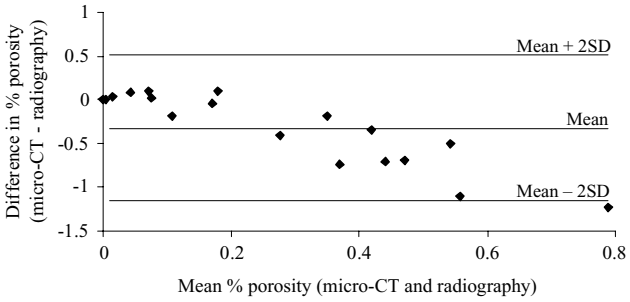

Fig. 2 Agreement between micro-CT and radiography.

3. Results

Mean disc porosity values for each of three measurement techniques are presented in Table 1. The precision of each technique is indicated in Table 2. The micro-CT technique was found to be the most repeatable, exhibiting a standard deviation approximately four times lower than those of the other two methods. When the threshold was altered by ± 10%, the difference in the calculated porosity was also significantly lower for the micro-CT technique. The radiographs were found to be highly sensitive to changes in threshold.

To assess agreement between micro-CT and each of the 2D techniques, the difference between measured porosities for each of the eighteen cement discs was plotted against the mean value of the data pair (Figs. 2 and 3). Generally, there was poor agreement between micro-CT and both 2D techniques with the difference between porosity measurements of the same order as the mean. In addition, agreement between techniques was found to worsen with increasing porosity. The negative mean difference (bias) found in both plots indicated that micro-CT gave a consistently lower measured porosity than the 2D techniques for specimens with a porosity greater than approximately 0.2%.

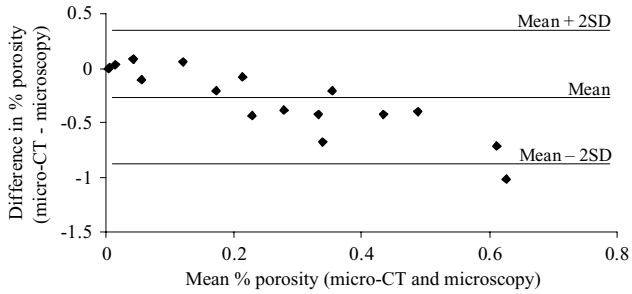

Fig. 3 Agreement between micro-CT and microscopy.

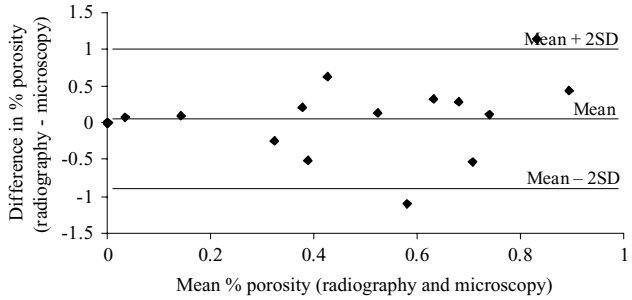

Fig. 4 Agreement between radiography and microscopy.

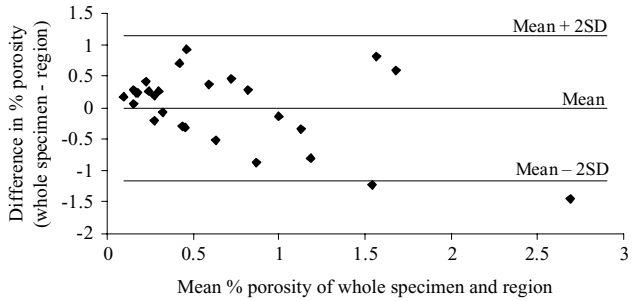

Fig. 5 Agreement between micro-CT whole specimens and micro-CT disc regions.

Comparison of the two 2D techniques (Fig. 4) also showed poor agreement that worsened with increasing porosity. The difference between porosity measurements was again of the same order as the mean porosity, in fact, in this case the limits of agreement (±2 standard deviations) were actually greater than the highest mean measured porosities.

The difference between the micro-CT measured porosity of the whole specimens and each of their three regions was plotted against the mean of the two measurements as shown in Fig. 5. The poor agreement found indicated that sample regions would not reliably represent the porosity of a whole structure.

4. Discussion

Micro-CT is increasingly being utilised to provide a powerful approach to the quantitative microstructural analysis of a wide variety of biomaterials. Given that the availability of

this technology is only relatively recent, this study was carried out in order to compare it with traditional techniques for bone cement porosity measurement that rely on predicting a 3D structure from a 2D surface.

Following the porosity measurement of eighteen bone cement specimens, poor agreement was found between all measurement techniques with the difference between measured porosities being of the same order as the mean. Micro-CT was found to be significantly more repeatable and less sensitive to changes in threshold than either of the 2D techniques. Therefore, the negative bias found between the micro-CT and 2D techniques was considered to be immaterial and was attributed to operator judgement in selecting thresholds. That is, the bias could equally have been found to be positive if the operator were to have chosen slightly different threshold values for the two 2D techniques.

Although the two 2D techniques had a nominally higher resolution (4×4 μm pixel size), the image manipulation and processing techniques resulted in some loss of quality such that the smallest pores detected were of the order of 50 μm diameter, which is similar to the smallest pores detected using micro-CT (20 μm diameter). It is assumed therefore, that the difference in porosity measurement results are not due to the superior resolution of one particular measurement technique. Micropores with a diameter smaller than 20 μm are unlikely to be detected using any of the measurement techniques described in this study.

Both 2D techniques were found to have limitations in measuring the bulk porosity of bone cement. In the case of high-resolution radiography, pores through the disc cross-section were superimposed onto a 2D surface, resulting in a mottled image with no clear pore boundaries. The porosity level measured was therefore highly dependent on the threshold value chosen. With microscopy, the large difference in values obtained from either surface of the same disc indicated that the porosity of a whole cement specimen could not be reliably predicted from a single surface. It is probably for these reasons that previous studies have often used either a combination of radiography and microscopy [4, 7, 16, 17], or only microscopy [3, 5, 8, 9, 11, 15] where reasonably precise area porosity measurements are taken from one surface and homogeneity is assumed.

A eliable quantification of bulk porosity is important when considering the fatigue strength of a particular bone cement. However, the overall poor precision of the traditional porosity measurement techniques and their lack of agreement suggests that this cannot be consistently determined from 2D measurements. In addition, the poor agreement between the whole specimen micro-CT data and the disc regions implies that the pore distribution in bone cement is largely inhomogeneous. Therefore, it appears to be necessary to analyse a much larger proportion of a specimen if the bulk porosity is to be reliably determined.

In a recent finite element study, Janssen *et al*. [22] confirmed the contradictory effects that pores may have on fatigue crack propagation [20]. They also demonstrated that the effect of porosity is determined only by the location of pores in the cement stress distribution and may be independent of the pore size and level of porosity. This finding is in agreement with clinical results that have found little evidence to suggest reducing the porosity of bone cement will increase implant life [23]. It is only through adopting a 3D measurement technique, like the one put forward here, that this crucial information on the distribution of pores in bone cement may be established. The fact that micro-CT is a non-destructive imaging technique makes it particularly suited to multiple applications such as the porosity measurement and evaluation of intact cement-bone constructs. However, imaging cement-prosthesis constructs could potentially be problematic where the prosthesis is metallic because of x-ray scatter.

5. Conclusion

This study has demonstrated that micro-CT provides an improved means of measuring bone cement porosity over traditional 2D techniques. Furthermore, it as been shown that measurement of a large proportion of a specimen is required to reliably determine bulk porosity. Recent literature surrounding the measurement of bone cement porosity supports the use of this new suggested technique, where a reliable and precise evaluation of the number, size and distribution of pores in bone cement could be used to improve future studies correlating porosity with implant life. The benefits of micro-CT have been previously recognised for evaluating the microstructure of many biomaterials. Therefore, from a progressive perspective, other future areas of research involving bone cements should also adopt this new technique wherever possible.

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