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MWCNT Used in Orthopaedic Bone Cements

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1. Introduction

This chapter discusses the use of carbon nanotube (CNT) based nanocomposites for biomedical applications, particularly in the area of orthopaedic bone cement used in joint replacement surgery.

The chapter initially introduces total joint replacements and poly methyl methacrylate (PMMA) bone cement. The associated issues and drawbacks with the use of these PMMA bone cements in terms of mechanical and thermal properties are then discussed in detail. The application of various MWCNT types (in terms of chemical functionality) at various weight loadings in augmenting some of the issues described is then presented. The next section of this chapter discusses the biological response to the various nanocomposite bone cements with MWCNT. The chapter concludes by discussing issues of CNT interaction with the body, and outlines the current trends in tagging and tracking the movement of MWCNT.

2. The hip joint

The hip joint (Figure 1) is a synovial ball and socket joint allowing for rotation about three perpendicular axes. It is constructed of the femoral head and the acetabulum of the pelvic bone. The femoral head and acetabulum are covered by cartilage. In a healthy hip joint the cartilage acts as a protective cushion to allow smooth movement of the joint, thus reducing friction and to some extent absorb shock. The presence of the synovial membrane secretes synovial fluid into the joint in order to nourish and lubricate the articulating cartilage (Martini and Bartholomew, 2000). The hip joint is responsible for the transfer of weight from the leg to the body, and as such, can be under substantial mechanical stresses.

2.1 Potential problems with the hip joint

Problems with the hip joint can arise due to cartilage damage within the joint caused by disease, trauma, or congenital conditions. This can lead to the surrounding tissues becoming inflamed, causing considerable pain.

Arthritis (joint inflammation) is the main cause of hip joint degradation (Havelin *et al.* 2003; Malchau *et al.* 2002). There are more than one hundred rheumatic diseases that can cause chronic pain, stiffness, and swelling in the synovial joints. The Arthritis Research

Campaign (ARC 2002) reported that in the UK, 206 million working days were lost due to arthritis and joint related conditions. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS 2004) stated that two of the most common forms of arthritis are osteoarthritis and rheumatoid arthritis. Primary osteoarthritis is a result of the gradual eroding of the cartilage layer (Figure 2a). It most commonly affects those over the age of 60 (ARC 2002) and remains the most common cause for primary joint surgery (94% of patients in 2005 (NJR 2006)). Congenital conditions such as a deformed joint or defective cartilage can result in osteoarthritis; however obesity, joint fracture, ligament tears, or other injury can damage cartilage, resulting in secondary osteoarthritis. It is noteworthy that while increased occurrences of osteoarthritis are indicative of an aging population, obesity is currently a major risk factor of osteoarthritis (ARC 2002). Overall, it is clear that osteoarthritis is the most common indication for joint replacement irrespective of age (Furnes *et al.* 2005; Karrholm *et al.* 2008; NJR 2006).

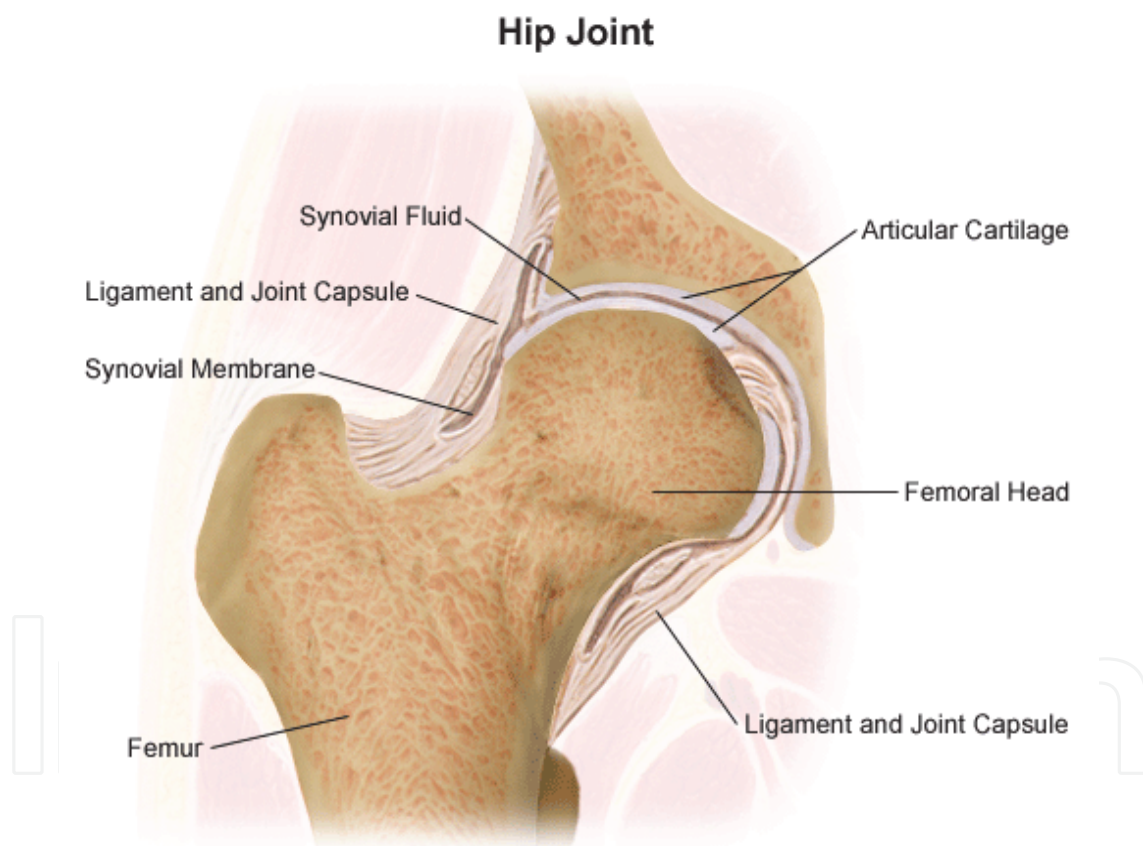


Fig. 1. Anatomy of a healthy hip (Martini and Bartholomew, 2000).

Rheumatoid arthritis is a chronic inflammatory disease of the joints whereby the synovium within the joint becomes inflamed. This inflammatory process damages the surrounding bone and cartilage (Figure 2b). Rheumatoid arthritis most commonly occurs during middle age of adulthood; however the disease can affect children and young adults as well. Rheumatoid arthritis usually affects joints symmetrically and most frequently attacks the hands, wrists, elbows, shoulders, knees and elbows.

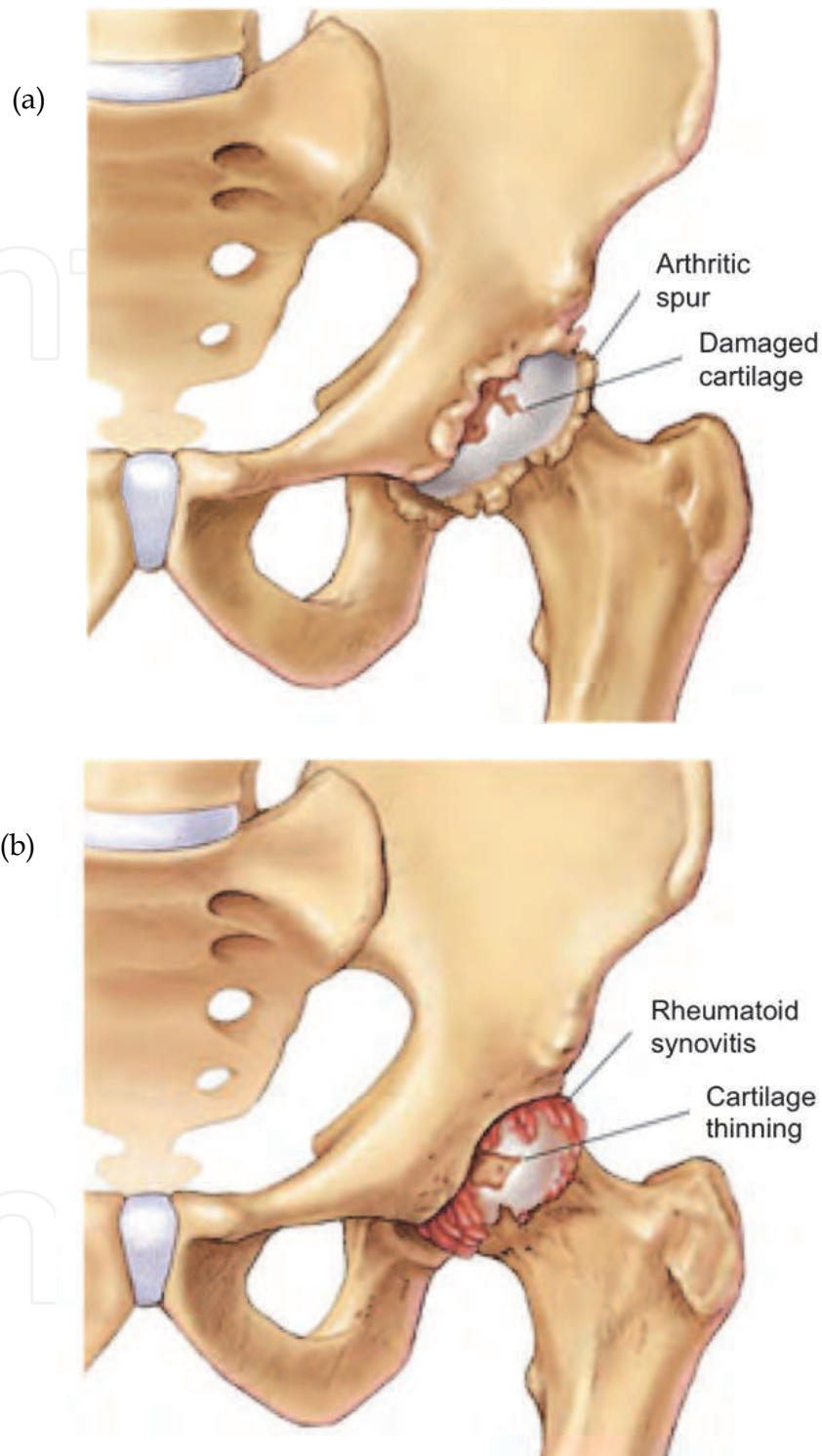


Fig. 2. Illustration of (a) Osteoarthritis and (b) Rheumatoid arthritis of the hip (Zimmer Inc., 2010)

2.2 Primary joint replacement

It is estimated that more than 29% of the population in the UK, are affected by arthritis and joint pain (ARC 2002). If partial damage of the joint has occurred, it may be possible to

repair or replace just the damaged areas; if the entire joint is damaged, however, a total joint replacement (TJR) may be necessary to relieve pain and to maintain function of the joint (Prendergast 2001). When replacing a total joint, the diseased or damaged parts are removed and artificial parts, i.e. prostheses or implants, are fitted. Due to the associated risks of surgery, in addition to high financial cost (in 1999-2000, hip and knee replacements alone cost the UK's health and social services £405 million (ARC 2002)), TJR is considered the last resort after failure of non-surgical treatment (Felson *et al.* 2000). TJR may be performed on a variety of joints, including hip, knee, ankle, shoulder, elbow, fingers and wrist. However, hip replacements are by far the most common, as reported, for example, in Norway between 1987 and 2004 (Furnes *et al.* 2005). Figure 3 shows an example of total hip replacement (THR) components.



Fig. 3. (a) Typical components of a total hip replacement (THR) and (b) the components *in vivo* (Smith and Nephew Inc., 2008)

During TJR, the most commonly used method of implant fixation is with a load transferring grout-like material, typically an acrylic based bone cement. The major advantage of these cemented joint replacements is the reduced operation recovery time: once polymerised the cement is capable of bearing load and offers immediate stability (figure 4).

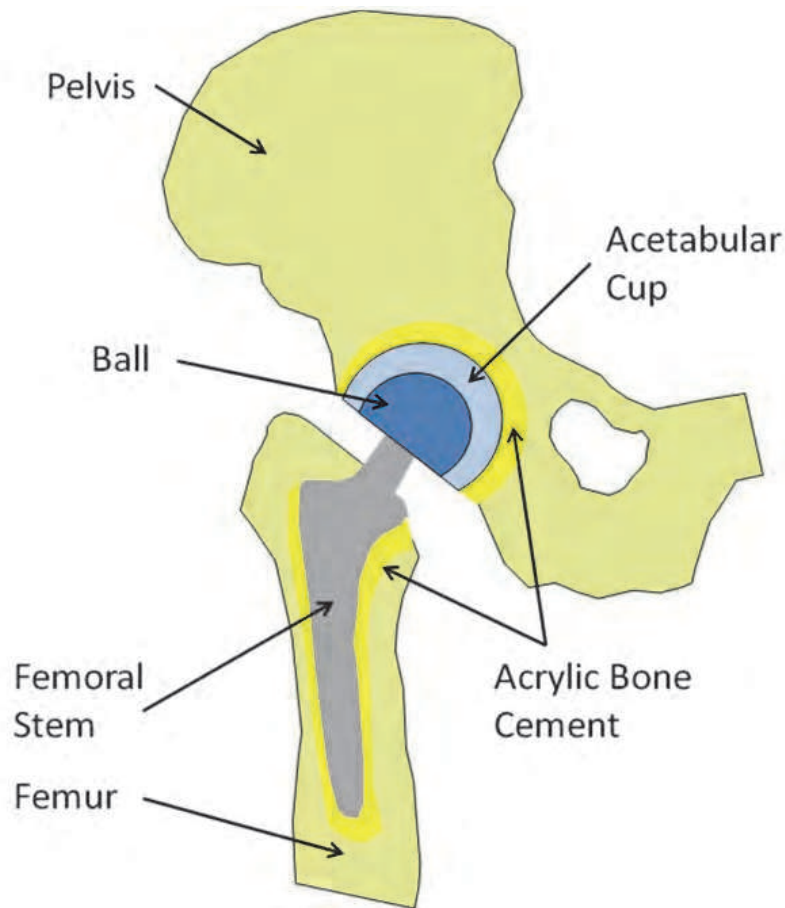


Fig. 4. Schematic diagram of a cement TJR.

However, if the cement mantle becomes loose, the surrounding bone may resorb and ultimate failure of the implant may occur. Uncemented implants were introduced to overcome these shortcomings, for example, cement wear particles, in addition to residual monomer and the highly exothermic polymerisation causing cellular necrosis to the surrounding bone. Uncemented implants typically use a roughened porous surface to promote bone growth around the prosthesis (Hungerford and Jones 1988). However, the bone cavity produced during the operation needs to be precise to ensure the implant is initially held in place through an interlocking mechanical fixation between the implant and the bone. It is also essential that the surrounding bone is healthy to enable this technique to be successful. In addition, the recovery time is long as the bone is required to regenerate. A combination of cemented and uncemented implants is also employed and often termed a 'hybrid'. More recently, resurfacing arthroplasty has been introduced, where less of the bone is removed compared with conventional TJR. Resurfacing procedures not only require the removal of less bone, but cause fewer complications during revision surgeries because the femoral canal is retained intact (Amstutz *et al.* 1998). On average, the number of primary arthroplasties in developed nations is increasing each year (Furnes *et al.* 2005; Karrholm *et al.* 2008; NJR 2006). Figure 5 demonstrates the proportion of cemented, uncemented and hybrid replacements. It is obvious from this graph just how much more popular cemented procedures are. It should be noted that the total number of TJRs performed in England and Wales is significantly greater than Sweden and Norway. In 2004, for example, 48,987 THRs

were recorded in England and Wales, compared to just 13,366 in Sweden and 7,061 in Norway. It should also be noted that the population of England and Wales (approximately 55m) is significantly greater than Sweden and Norway (approximately 13m). This equates to approximately 1 in every 1100 people in England and Wales, and 1 in every 650 people in Sweden and Norway.

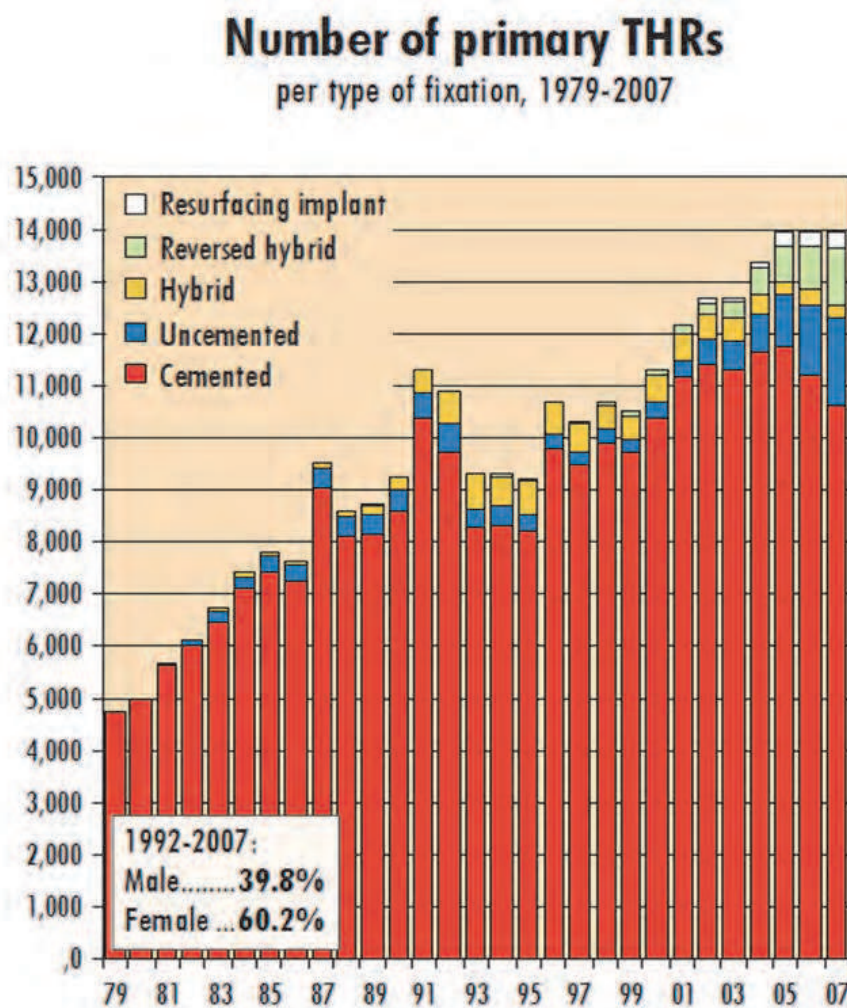


Fig. 5. Number and fixation type of primary THRs performed in Sweden from 1979 to 2007. (Karrholm *et al.* 2008)

Fully cemented TJR remain the most frequently used implant fixation procedure with 51% of primary THR in England and Wales being cemented in 2005, compared with 54% in 2004. In contrast, there was a slight increase in the application of bone cement for other fixation surgical procedures (NJR 2006). Alternative studies have shown that use of primary cemented TJRs over the last 10 years has remained consistent, whilst the application of cementless implants has almost doubled over the same period (Karrholm *et al.* 2008). This may be partly explained by the increase in the number of TJRs required for a younger age group (<60 yrs and <55 yrs for Sweden and England/Wales respectively). This cohort received more surgical procedures involving uncemented and hybrid implants (Karrholm *et al.* 2008; NJR 2006). It is important to note that whilst there is a slight decrease in the use of cemented implants in THR procedures; bone cement is still required for the majority of

implant procedures. In 2005, cement was used for the fixation of 73% of femoral stems and 53% of acetabular cups, in England and Wales (NJR 2006).

2.3 Acrylic bone cement

Poly (methylmethacrylate) (PMMA) has been used in orthopaedics since the early 1960s (Charnley 1960). It was first introduced by Sir John Charnley and Dr Dennis Smith. Also known as acrylic bone cement, it acts as a grouting agent for the fixation of artificial joints as well as the treatment of spinal compression fractures (vertebroplasty). In TJR, bone cement fills the space between prosthesis and bone and acts as an elastic buffer, therefore transferring mechanical load on the implant to the bone. This function of distributing stresses is critical for implant longevity. If the external stresses exceed the ability of the cement to transfer the load, a fracture results (Kuehn *et al.*, 2005).

Acrylic bone cement is a two phase system, consisting of a polymer powder and monomer liquid. The powder phase primarily consists of spherical PMMA beads (82–89 wt. %), in addition to an inorganic radiopacifying agent, usually barium sulphate or zirconium dioxide (10 – 15 wt. %). The powder component also contains benzoyl peroxide (BPO; 0.5–2.6 wt. %), which catalyses polymerisation. The liquid phase is largely MMA monomer (98 wt. %), with 2 wt. % N, N-Dimethyl-*p*-toluidene (DmpT) which accelerates the polymerisation. From a chemical point of view, MMA is an ester of methacrylic acid with a polymerisable double bond. When the liquid and powder phases are mixed, the initiator (BPO) reacts with the accelerator (DmpT) to form free radicals in what is known as the 'initiation reaction'. These free radicals initiate polymerisation of MMA into PMMA by adding to the polymerisable double-bond of the monomer molecule. Temperatures during this reaction can reach up to 110°C. During polymerisation, the bone cement is worked into a 'dough' phase that can be moulded or injected. In a relatively short amount of time (10 – 15 minutes) the bone cement hardens to ca. 90% of its final mechanical properties (Kuehn *et al.*, 2005). Although current revision rates of cemented TJR are low, improved mechanical and thermal properties are required to further reduce subsequent surgeries of cemented arthroplasties, and increase the longevity of the implant. With 88.7% of current cemented implants expected to last at least 14 years (Karrholm *et al.* 2008), this would mean that more physically active patients would have to undergo a number of revision surgeries in their lifetime. Furthermore, younger patient populations are more likely to impose heavier, more complex loadings on the implant, as they would wish to continue pursuing an active lifestyle.

3. Composition and polymerisation reaction

3.1 Composition

Acrylic bone cement, as mentioned is primarily composed of poly methylmethacrylate (PMMA). Most commercial acrylic bone cements comprise of a two part self-curing acrylic polymer, usually formulated as a 2:1 powder to liquid ratio. These components are mixed immediately prior to implantation during surgery and delivered directly to the implant site. The compositions of the main commercial bone cements are summarised in Table 1.0, showing variations in chemical composition. Other cements may also contain antibiotics (e.g. gentamicin sulphate (Lewis 2003; Hendriks *et al.* 2004)) in order to improve the body's response to the implant, reducing risk of subsequent infection and implant rejection.

Constituent	CMW-1	CMW-3	Palacos R	Simplex P	Zimmer LVC
POWDER COMPONENTS					
Benzoyl peroxide (BPO)	2.60	2.20	0.5-1.6	1.19	0.75
Barium sulphate (BaSO ₄)	9.10	10.00	-	10.00	10.00
Zirconium dioxide (ZrO ₂)	-	-	14.85	-	-
Chlorophyll	-	-	200 ppm	-	-
PMMA	88.30	87.80	-	16.55	89.25
PMMA-Methacrylic acid (P(MMA/MA))	-	-	83.55-84.65	-	-
PMMA- <i>styrene</i> copolymers P(MMA/ST)	-	-	-	82.26	-
LIQUID COMPONENTS					
NN Dimethyl P Toluidine (DmpT)	0.40	0.99	2.13	2.48	2.75
Hydroquinone	15-20 ppm	15-20 ppm	64 ppm	75 ppm	75 ppm
Mehtylmethacrylate (MMA)	98.66	98.07	97.87	97.51	97.25
Ethanol	0.92	0.92	-	-	-
Ascorbic Acid	0.02	0.02	-	-	-
Chlorophyll	-	-	267 ppm	-	-
Gentamicin sulphate	-	-	-	-	-

Table 1. Compositions of six commercial formulations of bone cement (Lewis 1997). The compositions are given in percent (w/w) except where stated otherwise.

3.2 Polymerisation reaction

PMMA is an amorphous polymer, which is plasticised on the addition of the monomer methyl methacrylate (MMA). When bone cement is mixed two processes occur, firstly the monomer is absorbed by the PMMA beads and secondly, a free radical polymerisation reaction occurs (Kuehn *et al.* 2005). This reaction is shown schematically in Figure 6 below. During this reaction the DmpT causes the BPO to decompose leaving a benzoyl radical, and a benzoyl anion (Figure 6a). These benzoyl radicals then initiate the polymerisation of the MMA by combining and forming an active centre (Figure 6b). These active centers then combine with multiple molecules to form a polymer chain (Figure 6c). This reaction forms a viscous fluid allowing the polymerising cement to be moulded as required, i.e. this is the stage when the surgeon would inject the bone cement into the prepared bone canal prior to implanting the stem. As the monomer begins to polymerise, the cement hardens around the stem, holding it in place. This reaction is highly exothermic, an example of a temperature plot of bone cement during polymerisation is shown in Figure 7. The heat energy produced during polymerisation is 57 kJ per mole MMA, resulting in temperatures, which can exceed 100°C. These elevated temperatures can cause cellular bone necrosis which can ultimately contribute to aseptic loosening (Dunne and Orr 2002; Stanczyk and van Rietbergen 2004; Kuehn *et al.* 2005). It should be noted though that the polymerisation temperatures experienced *in vivo* have been much lower (between 40–47 °C) at the bone interface (Toksvig-Larsen *et al.*, 1991). This is due to the reduced thicknesses of bone cement mantle, the presence of blood circulation, and the dissipation of heat through the implant and

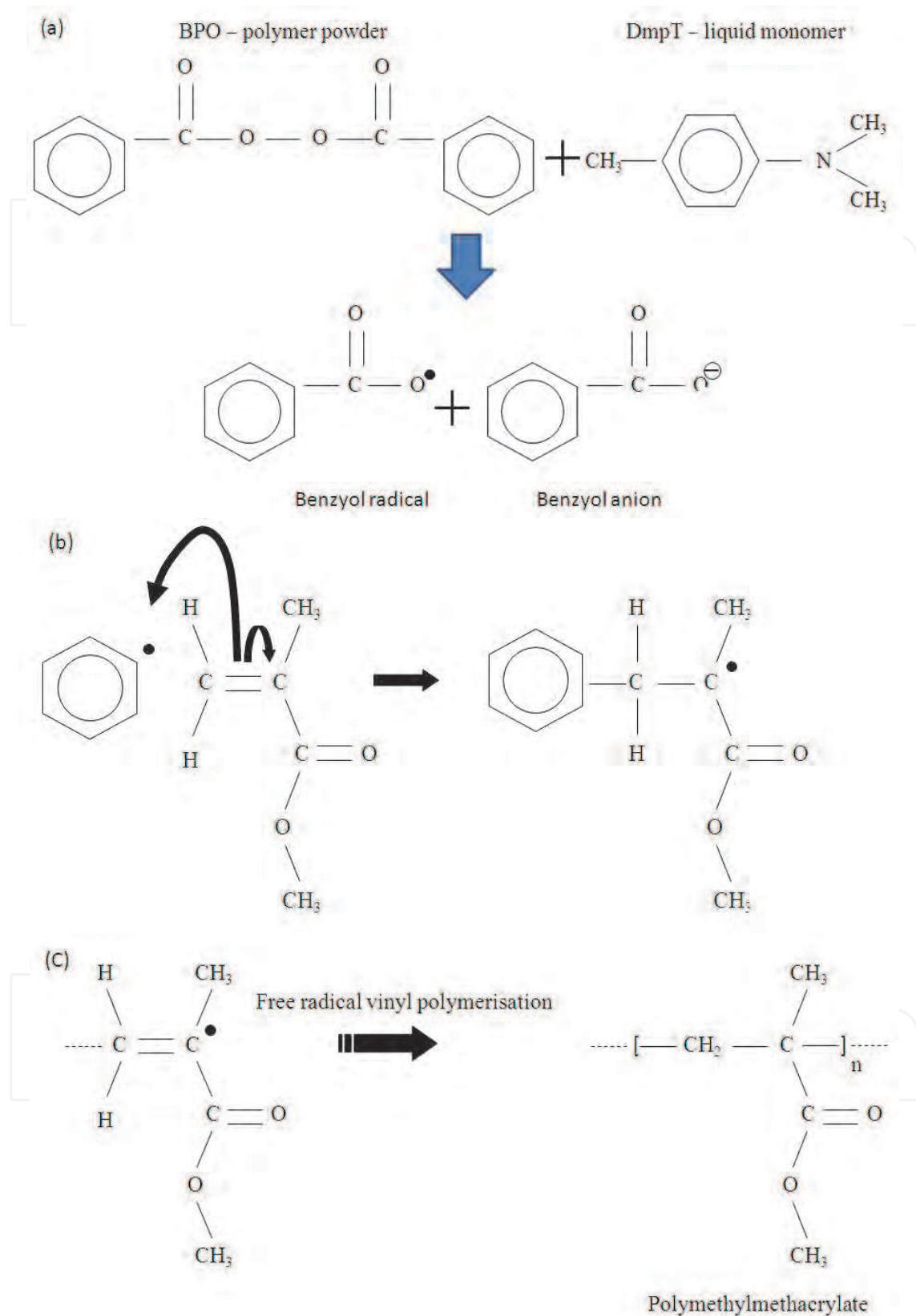


Fig. 6. (a) Schematic diagram showing the decomposition of BPO leaving a benzoyl radical, and a benzoyl anion; (b) How these benzoyl radicals initiate polymerisation of MMA; (c) formation of a polymer chain.

surrounding tissue (Kuehn *et al.* 2005). It has been shown that volumetric shrinkage can occur due to thermal contraction on cooling and the changing density as polymerisation progresses (Gilbert *et al.* 2000; Kuehn *et al.* 2005). Gilbert *et al.* (2000) reported that volumetric shrinkage as a result of density variation, due to the exothermic polymerisation was between 5.1 % and 6.5 % depending on mixing method employed and type of cement. Both shrinkage mechanisms have been identified as factors which influence the levels of residual stresses within the cement (Gilbert *et al.* 2000; Orr *et al.* 2003).

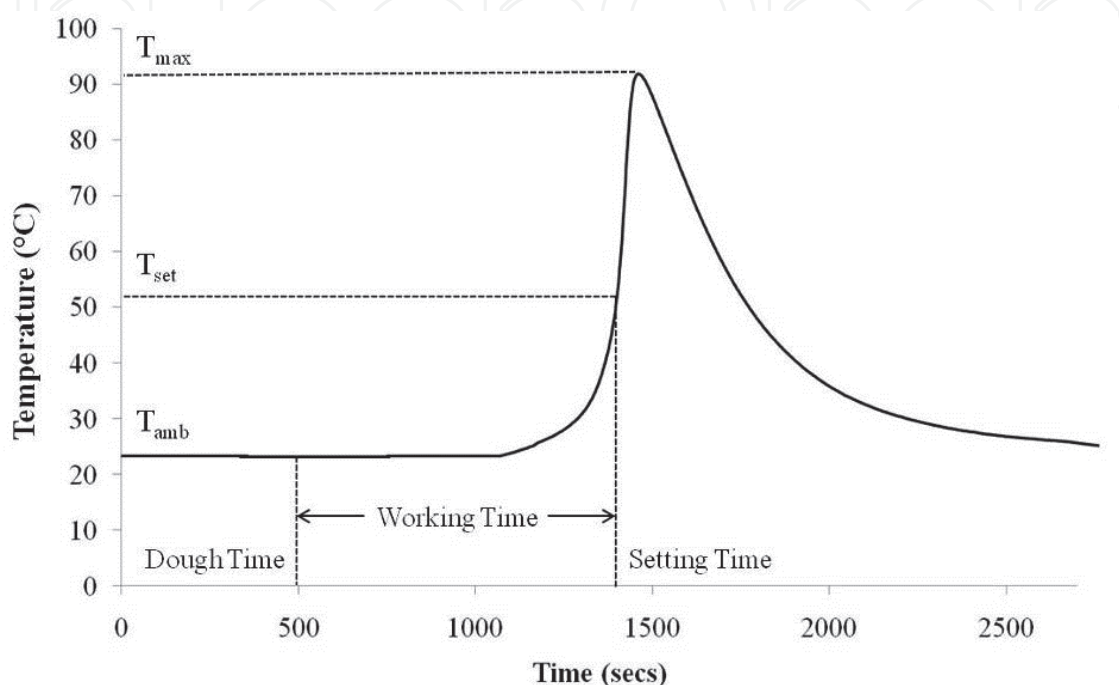


Fig. 7. A typical curing curve for acrylic bone cement where T_{max} is the maximum temperature reached, T_{set} is the setting temperature and T_{amb} is the ambient temperature.

As illustrated in Figure 7, the time that has elapsed after initial mixing when the cement takes a homogeneous dough-like state is known as the 'dough time'. This point may be identified with temperature or, average molecular weight of the polymer. However, as specified in the British Standard BS 7253 (ISO 5833:2002), it is the point at which the cement will no longer stick to powderless surgical gloves (typically 2-3 minutes after initial mixing). The time from the end of dough time until the cement can no longer be manipulated, is defined as the working time. During an operation this is the time during which the surgeon must insert the stem and adjust its position. Finally, the setting time is the time from the onset of mixing until the surface temperature reaches one half of the maximum temperature, as described in ISO 5833:2002.

4. Current issues with acrylic bone cement

4.1 Mechanical properties

The main role of bone cement is to transfer load between bone and the metallic prosthesis. Several studies have shown that the composition of acrylic bone cement significantly influences the mechanical properties of the cement (including Harper and Bonfield 2000; Lewis 2000). It is during the polymerisation process that numerous cement properties, for

example viscosity, setting time, maximum cure temperature, and volumetric shrinkage etc, can be determined. These material characteristics may influence a cemented TJR performance. It has also been shown that the variability in the mechanical static and dynamic properties of commercial bone cements is significant, with greater relative differences reported in fatigue properties (Lewis 1997; Harper and Bonfield 2000). Harper and Bonfield (2000) found that there was some correlation between the static and fatigue strengths, however the ranking of the different cements tested did not match exactly. Mechanical properties are known to be affected by: cement composition, size and morphology of the PMMA beads, molecular weight, cement mixing technique, and the powder-liquid ratio (Harper and Bonfield 2000; Lewis 1997). The variation in tensile strength, for example, is reported to vary between 24–49 MPa for five different commercial bone cement formulations, depending on the mixing technique, specimen age and test conditions (Lewis 1997).

4.2 Thermal properties

As mentioned previously, *in vivo* temperatures during the exothermic polymerisation of bone cement can cause thermal necrosis (tissue death) of the bone cells and impaired local blood circulation, which can lead to early failure through aseptic loosening of the implant (Huang *et al.* 2005). It has been reported that for epithelial cellular death to occur, an exposure time of 1 s is required for temperatures above 70 °C, 30 seconds for temperatures greater than 55 °C, and approximately five hours for temperatures greater than 45 °C (Starke *et al.* 2001). Collagen protein molecules are denatured at 45 °C, and experience irreversible damage at 60 °C if held at these temperatures for an hour. It has also been reported that thermal necrosis occurs in bone tissue when exposure is greater than 1 minute for temperatures above 50 °C and denaturation of sensory nerves occurs for temperatures above 45 °C if exposure exceeds 30 minutes. The amount of heat generated during polymerisation is dependent on the amount of reacting monomer, however the maximum temperature reached is also dependent upon the rate of heat dissipation. *In vitro* testing completed by Stanczyk and van Rietbergen (2004) suggested that the tips of bone trabeculae protruding into setting cement may experience temperatures in excess of 70 °C. In the 1960s, upon first use of bone cement in TJR, Charnley believed that while temperatures of ~100 °C could be reached during polymerisation, in the presence of a metallic prosthesis, which would act as a heat sink, there was a reduction in the peak temperature experienced *in vivo*. (Charnley 1960). Since then, numerical simulations and *in vitro* studies of thermal necrosis and peak exotherms in TJR, have helped establish two methods which may assist the reduction of thermal necrosis: (a) the use of thin cement mantle layers, and (b) pre-cooling of the bone surface (Chandler *et al.* 2006; Fukushima *et al.* 2002).

An additional potential adverse consequence of using standard acrylic bone cements is the leaching of residual liquid monomer into the surrounding tissue, which may cause inflammation, chemical necrosis and even death. Average levels of residual monomer can be as high as 5%, however local concentrations may be as high as 15 %, increasing the likelihood of chemical necrosis (Stanczyk and van Rietbergen 2004). Vacuum mixing of acrylic bone cement has been associated with reduced levels of residual monomer as mixing bone cement at reduced pressures increases monomer polymerisation (Bettencourt *et al.* 2001).

There is considerable variation in the chemical composition of different brands of cement (Table 2.1). Often this difference involves more than one of the basic constituents, making it difficult to draw any conclusions regarding the effect of composition on mechanical

properties of the cement. It is accepted that the intrinsic properties of the monomer units and the high molecular weight dictate their subsequent mechanical properties such as craze strength, creep resistance and fatigue performance (Sauer and Richardson 1980; Hull and Clyne 1996a). Lewis (2003) reviewed the effect of molecular weight on fatigue performance of bone cement, reporting that increasing the molecular weight of either the powder or the fully cured cement improves the fatigue performance of acrylic bone cement, assuming all other parameters remain fixed. Lewis (2003) suggested that this increase in mechanical performance was related to the increase in polymer chain entanglement due to increased molecular weight which in turn, increased the resistance of the bone cement to craze formation and lead to subsequent increased fatigue crack propagation resistance (Sauer and Richardson 1980; Lewis 2000). Deb *et al.* (2003) reported that increasing the quantity of initiator and activator increased the peak temperature reached during polymerisation reaction and, in addition, lowered the setting time. The content of the residual monomer in the cured bone cement specimens was additionally determined, and it was reported that the highest concentrations of initiator and activator provided the lowest content of residual monomer. However, the concentration of these compounds within the cement must be controlled as they have detrimental health implications when released into the patient. It has also been shown that the type of activator used in polymerisation may significantly influence the fatigue life and fracture toughness of bone cement due to changes in the molecular weight of the resulting polymer (Deb *et al.* 2003). Residual MMA can result after incomplete polymerisation, and is known to influence the mechanical properties and fatigue performance of acrylic bone cement by acting as a plasticiser (Vallo *et al.* 1997; Lewis and Janna 2004). Unreacted MMA is also a possible source of toxicity in the surrounding tissue with possible effects such as hypotension, tissue irritation and alveolar lesions. It has been seen that complete polymerisation and therefore minimal residual MMA content, can be ensured by selecting a suitable initiator activator ratio without significantly affecting fracture toughness (Hasenwinkel *et al.* 2002). Alternatively, the presence of residual monomer can reduce the amount of shrinkage of the bone cement, assuming no other sources of shrinkage occur (Gilbert *et al.* 2000).

4.3 Fatigue failure of bone cement - *In vivo* analysis

Within a cemented implant femur, four main areas of weakness have been recognized as potential failure initiation sites, and can be identified as the: (1) cement, (2) bone-cement interface, (3) cement-prosthesis interface and (4) host bone. Jasty *et al.* (1991) used fractographic analysis to examine *ex-vivo* femoral components, reporting evidence of de-bonding at the cement-prosthesis interface in the majority of the TJR investigated. Partial or complete fracture of the cement mantle was frequently coupled with de-bonding at the cement-prosthesis interface. In the early stages of failure, micro-cracking was evident at the cement-bone interface, although these micro-cracks were considered to be non-critical events as there was no evidence to suggest they were associated with complete fracture across the cement mantle. Fatigue damage accumulation is therefore common prior to overall loosening of the implant *in vivo*. Cemented hip replacements typically experience final failure after several fracture sites have developed, although single, longitudinal cement fractures causing loosening, and subsequent failure have also been recorded *in vivo* (Jasty *et al.* 1991; Topoleski *et al.* 1990). As mentioned previously, fractographic analysis performed on *ex-vivo* specimens of failed bone cement has allowed *in vivo* failure mechanisms to be observed and, as a result, several groups have demonstrated that *in vitro* testing can

replicate the micro-mechanisms of failure *in vivo* (Topoleski *et al.* 1990/1993; Verdonchot and Huiskes 1997a; Murphy and Prendergast 2002).

Typically, fracture surfaces were identified with a stepped or irregular fatigue region, this region then evolved into a flat, rapid fracture region (Topoleski *et al.* 1990). This stepped or irregular surface can be attributed to the coalescence of micro-cracks that have formed ahead of the crack tip during crack propagation. Initiating micro-cracks (Figure 8) were believed to exist as a result of internal defects such as pores, aggregates of the radiopaque agent, inclusions from the bone at the bone-cement interface, residual stress-induced cracks at the cement-prosthesis interface, and implant design (Jasty *et al.* 1991; Bishop *et al.* 1996; McCormack and Prendergast 1996; Orr *et al.* 2003; Prendergast 2001b; Murphy and Prendergast 2002).

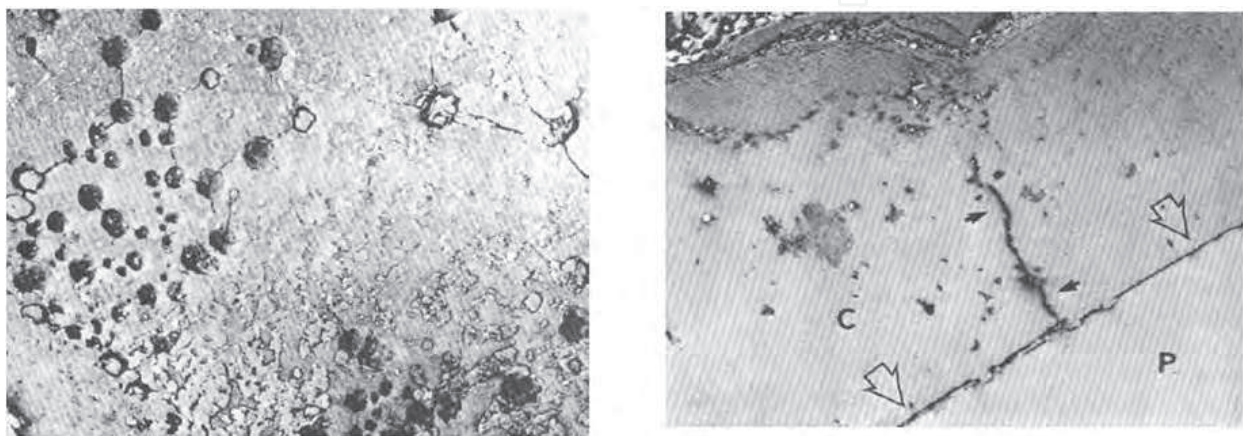


Fig. 8. Scanning electron micrographs showing (a) micro fractures through pores near distal end of prosthesis and (b) an incomplete fracture through the cement mantle originating at the cement-prosthesis interface, Jasty *et al.* (1991).

McCormack *et al.* (1998) used experimental and finite element modeling of the cemented construct to complete statistical analysis of micro-crack accumulation. Representation of micro-crack initiation and propagation was achieved for a longitudinal cross-section of the implanted construct. This allowed for the modeling of the bone-cement and cement-prosthesis interactions. The damage accumulation was found to vary significantly over different regions of the cement mantle. It was reported that more significant cracking occurred at the lateral side of the cement mantle compared with the medial side, however an increased rate of crack formation was seen at the distal end (*cf.* proximal), with more cracks initiating from the bulk of the cement (*cf.* the interfaces). It was also noted that a greater incidence of cracks originating from the bone-cement interface was seen to occur compared to the cement-prosthesis interface. Alternative studies have reported that the location at which a fracture initiates depends on the type of loading applied to the specimen. McCormack and Prendergast (1999) reported a greater occurrence of fatigue cracks initiated from pores within the cement mantle when examining cement under bending loads. Under torsional loads, they observed that cracks initiated most often at the interfaces (McCormack *et al.* 1999). Additionally, as previously mentioned in a study by Jasty *et al.* 1991, *ex-vivo* observations reported evidence of cracks initiating from the cement-prosthesis interface and from voids within the bulk of the cement, suggesting both crack growth scenarios may be important. Prendergast (2001b) confirmed the dependence of crack initiation on loading type, and also suggested that in order to reduce this damage accumulation, the volume of

cement stressed to a critical degree must be minimised. There is some disagreement as to the predominant source of fatigue damage accumulation; *in vitro* test specimens demonstrate the benefits of a reduced porosity within the cement (Dunne *et al.* 2003). However, the associated complexity of the *in vivo* cement mantle, in addition to the stress singularities introduced at sharp corners of the implant, and the cement interfaces, may over-shadow the stress amplifying effect of porosity (Janssen *et al.* 2005b). It is however, widely accepted that porosity has a marked influence on damage accumulation, as pores have the potential to act as initiation sites or aid crack coalescence. It should be noted that failure of the cemented construct is not just influenced by damage accumulation and final fracture of the cement mantle. Wear particles associated with the breakdown of cement during de-bonding and fracture, may be transported throughout the implant, leading to an immune-response and the development of osteolysis. Resultant bone degradation will ultimately lead to aseptic loosening of the implant (Anthony *et al.* 1990). A further feature of bone cement is its ability to creep under sustained loading (either static or fatigue), which may contribute to damage development over time. The relationship between creep and damage accumulation is complex. Creep is thought to promote stress relaxation within the cement mantle, reducing the damage accumulation rate (Stolk *et al.* 2004). However, it may also serve to increase levels of implant migration, but the magnitude of this has been shown to be insignificant (Verdonschot and Huiskes 1997b).

4.4 Mechanisms of failure in bone cement – *In vitro* analysis

4.4.1 Fatigue crack initiation

In vitro strain measurements completed by O'Connor *et al.* (1996) have shown the variation in stresses within the cement mantle. The presence of stress raisers within the cement mantle (e.g. porosity) have the potential to sufficiently raise stresses and cause fatigue crack initiation, and subsequent failure. Whilst extensive research has been conducted on the factors that cause crack initiation, a full understanding of the micromechanics involved is yet to be achieved (Lewis 2003). *In vitro* studies by Orr *et al.* (2003) suggested that cracks may be present prior to the loading of the implant, i.e. once the cement has polymerised. Whether cracks are more likely to occur at the bone-cement interface or at the cement-prosthesis interface is a source of discussion. Bishop *et al.* (1996) reported that pores may be more likely to occur at the cement-prosthesis interface due to the presence of a temperature gradient. If a prosthesis conditioned at room temperature is implanted into bone at body temperature, the polymerisation process will begin at the bone-cement interface, hence the cement-prosthesis interface will polymerise later. Porosity at the cement-prosthesis interface due to cement shrinkage will cause reductions in the static and dynamic properties. In contrast, Orr *et al.* (2003) reported that voids and micro-cracks are more likely to occur at the cement-bone interface due to the presence of residual stresses caused by thermal shrinkage around the metallic implant, with a small proportion of cracks initiating from pores within the mantle. McCormack and Prendergast (1999) proposed that initial levels of new crack initiation are higher early on in the loading history, due to stress relief occurring at regions of stress intensity. Furthermore, McCormack and Prendergast (1999) suggested that crack growth rate is the same for all types of micro-cracks, whether “pre-loaded” (i.e. cracks formed as a result of stress relief during cement shrinkage or, from regions of high stress concentration) or ‘load-initiated’ (i.e. cracks formed due to fatigue loading). As a result it is believed that pre-loaded cracks play a critical role in the aseptic loosening process and thus, the overall failure of cement mantle. Any improvement made to the mixing process

(reduction in porosity) and to the level of shrinkage during polymerisation, may then, in theory, impede levels of damage accumulation.

4.4.2 Fatigue crack growth

Fatigue crack growth can propagate in two different phases and are typically observed as a flat, rapid fracture region preceded by an irregular, or stepped fatigue region (Topoleski *et al.* 1990). The stepped or irregular region, is representative of the early stages of slow crack growth, and may be accounted for in polymers by a process known as “discontinuous crack growth” (DCG). DCG refers to a single burst of fatigue crack advance after several hundred fatigue cycles (Takemori 1984). At high stress intensity factors (ΔK), striated growth usually occurs at the crack tip. Striations refer to the growth bands visible on a fracture surface whose spacing is equivalent to crack growth rate per stress cycle. Striations are orientated perpendicular to the direction of crack growth. Striations are often confused with DCG bands, with the main differences being that the DCG band spacing is significantly greater than the crack length increment per cycle and these bands arise at low ΔK values. Once crack initiation has occurred, it will be in the DCG regime, and the mechanisms by which the crack develops throughout this regime will ultimately determine the fatigue crack growth resistance of the material (Takemori 1984). Fractographic studies have shown that DCG is of relevance for acrylic bone cement with distinct bands being observed in *ex-vivo* samples (Jasty *et al.* 1991; Topoleski *et al.* 1990). DCG is a function of the testing and specimen preparation conditions, environmental effects and compositional changes, all factors that influence the fracture properties of the polymer (Takemori 1984). Changes to the bone cement that influence these factors must be carefully considered with respect to their affect on the overall structural performance of the cement. During the early stages of fatigue crack propagation, DCG band formation is favoured by the development and growth of crazes ahead of the crack tip (Skibo *et al.* 1977). Crazes are identifiable as dense arrays of fibrils inter-dispersed with elongated voids that appear ahead of the crack tip, effectively reducing the density of the polymer in that region. Crazes are generally perpendicular to the applied stress, which result in inelastic deformation by craze widening in the local principal stress direction. In amorphous glassy polymers (e.g. PMMA) brittle fractures occur through crazing and crack propagation (Scheirs 2000b). Crazing has been reported in detail for PMMA by Pulos and Knauss (1998a/b/c). Pulos and Knauss (1998a/b/c) described how damage (identifiable with crazing) ahead of the fatigue crack tip may occur over many cycles, causing a sudden jump in the crack. As mentioned previously, crazing is prominent in polymers ahead of the crack tip at low ΔK values and DCG may occur within this craze zone once the maximum opening of the craze zone reaches a critical value (Figure 9).

Crazing is a common form of polymer deterioration. Crazing is often a precursor to crack growth and failure, however in thermoplastics the presence of crazing can aid fracture toughening. In these cases, the mechanism of crazing enables polymers to absorb energy through the matrix (in-elastic) deformation. This is possible because the energy used to initiate crazing, and crack growth is large and allows the energy to be dissipated over a large area (Luo *et al.* 2004; Topoleski *et al.* 1990). Alternatively, in thermosetting plastics, crazing may lower the strength of the polymer and lead to premature failure (Scheirs 2000b). Crack propagation through a polymer may also be retarded through crack bridging and, to some extent, micro-cracking; this effect may influence both static and

cyclic failure. Previous work in the literature suggests that secondary cracks are present in cement failure (a result of tensile stress relief) (Verdonschot and Huiskes 1997b), therefore consideration of these toughening mechanisms may be appropriate. Non-uniform extension of a crack tip can result in un-cracked ligaments. It should be noted that micro-cracks only act as a toughening mechanism when they are constrained; otherwise they are detrimental to the fracture toughness as they propagate and develop into long cracks (Nalla *et al.* 2004).

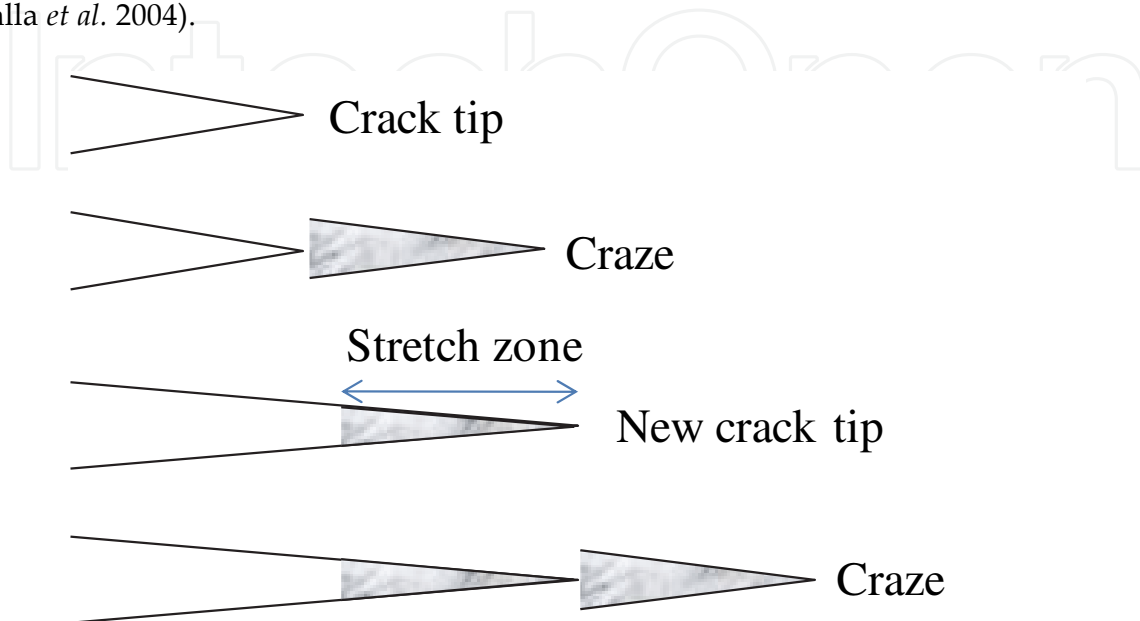


Fig. 9. Illustration of discontinuous band growth (DCG) within the craze zone, ahead of a crack tip.

4.5 Effect of residual stresses and cement shrinkage

It is well accepted that residual stresses are generated within the cement mantle following polymerization and have a direct influence on the stress distribution at the cement-prosthesis interface. Knowledge and understanding of these processes may allow a more accurate prediction of load transfer and in-service conditions in the cement mantle (Nuno and Amabili 2002; Nuno and Avanzolini 2002; Orr *et al.* 2003; Roques *et al.* 2004). Stresses due to shrinkage, exist in cement surrounding the stem in both the longitudinal and the hoop direction (Roques *et al.* 2004). These stresses will be at their greatest immediately post-operatively, with a reduction occurring with time as stress relaxation, and creep occur (Verdonschot and Huiskes 1997a; Nuno and Amabili 2002; Nuno and Avanzolini 2002; Stolk *et al.* 2004). This may create more favourable stress distributions at the interfaces between the cement-bone, and cement-prosthesis, as finite element modelling of bonded and unbonded stems predicts that an increase in compressive stresses at these regions may occur (Verdonschot and Huiskes 1997a). The presence of pores at either interface has been attributed to volume shrinkage of the cement during polymerization. Some polymerization shrinkage will occur while the cement is still viscous and hence can be accommodated by flow (Orr *et al.* 2003). However, as polymerization progresses, this flow may not accommodate shrinkage and cracks can initiate in high stress areas as a mechanism of stress relief. While residual stresses do exist in fully polymerized bone cement, the additional presence of porosity, high stress concentrations or excessive heat generated during polymerization may still be required for large cracks to initiate. As residual stresses alone

may not be enough to generate cracks (Lennon and Prendergast 2002). The ultimate tensile strength of various bone cements range between 24 and 49 MPa (Lewis 1997), whereas residual stresses of between 2.5 MPa (Nuno and Avanzolini 2002) and 12.6 MPa (Orr *et al.* 2003) have been reported. The direction in which the cement will shrink is of great significance. Orr *et al.* (2003) reported this has a direct relation to the levels of micro-cracking that may occur as a result of shrinkage stress, although the use of acoustic emission has provided evidence for the shrinkage of the cement onto the femoral implants (Roques *et al.* 2004). Furthermore, shrinkage is known to be affected by the volume fraction of monomer content (Gilbert *et al.* 2000).

4.6 The role of porosity

Lewis (1997) identified four main reasons why porosity occurs in bone cements;

- i. The entrapment of air between the polymer powder and monomer liquid as the powder is wetted by the monomer upon mixing,
- ii. Evaporation of the liquid monomer during polymerisation,
- iii. Entrapment of air during mixing,
- iv. Entrapment of air upon transfer of the dough into the cement gun (depending on mixing method).

Materials engineering principles and the relevant literature explain that the presence of pores within the cement mantle act as stress raisers, which may then act as crack initiation sites under applied loads. Many researchers have demonstrated that reduced porosity allows for improved compressive, flexural and fatigue properties of acrylic bone cement (Lewis 1997; Murphy and Prendergast 2000; Dunne and Orr 2002; Dunne *et al.* 2003), therefore the level of porosity (both macro- and micro-pores) should be minimised. Pores of diameter ≥ 1 mm are deemed macro-pores, and are generally introduced during the mixing process when air is trapped within the cement mixture. These macro-pores are often cited as being the cause of low fatigue life for test specimens as crack initiation is often associated with a single pore. Micro-pores have diameters ≤ 1 mm, and may be established due to the evaporation of the liquid monomer during the polymerisation process and/or entrapment of air during mixing (Dunne *et al.* 2003). It is often observed that multiple smaller pores (≤ 1 mm) in close proximity are more detrimental than one larger pore (≥ 2 mm); this is often a result of the type of mixing method employed (Murphy and Prendergast 2000). A multiple pore arrangement is typically observed for hand mixed specimens (Figure 10) where the combined interaction of the pores produces a stress concentration large enough to cause fatigue crack initiation. In contrast, vacuum mixing (Figure 11) usually generates a smaller distribution of pores. There is evidence to suggest that hand mixed cement reduces the level of shrinkage that cement experiences due to the high level of porosity introduced during mixing, (Dunne *et al.* 2003), as only the cement shrinks during polymerisation and not the voids (Kuehn *et al.* 2005). However, porosity may be beneficial to reduce residual stresses prior to loading; this benefit could be outweighed by the adverse effects observed for fatigue crack initiation and propagation. When the propagating crack tip reaches a pore, failure is considered to occur instantly across the void area, effectively causing the crack propagation rate to increase. Conversely though, there are studies that suggest that pores act as crack "blunters" thereby increasing the fatigue life of the bone cement (Topoleski *et al.* 1993), although crack acceleration into the void must also occur due to the local stress concentration at such a defect.

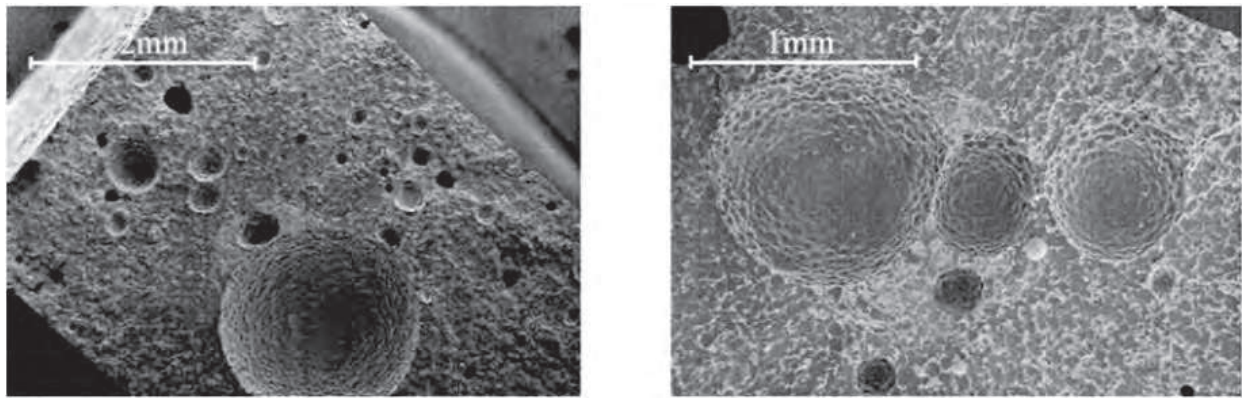


Fig. 10. Scanning electron micrograph of a hand-mixed fracture surface for commercial bone cement showing a large pore with a large number of small pores (Murphy and Prendergast 2000).

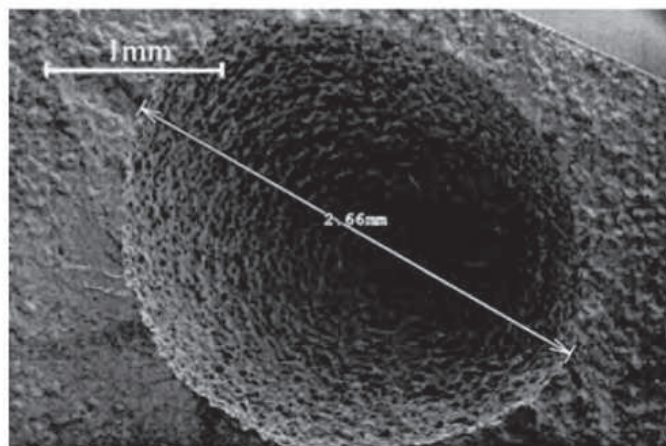


Fig. 11. Scanning electron micrograph of a vacuum mixed fracture surface of commercial bone cement, with a larger pore size compared to hand mixed cement (Murphy and Prendergast 2000).

4.7 Presence of radiopaque agent

Radiopaque agents are included in bone cement formulations (approximately 10-15 % wt.) to allow the cement to be distinguishable from the surrounding body tissues on radiographs. Barium sulphate (BaSO_4), Zirconium dioxide (ZrO_2) and iodine-containing copolymers are a few of the possible radiopaque agents used, however BaSO_4 is most commonly used. It has been reported that BaSO_4 particles do not influence the polymerisation reaction or handling properties of bone cement (Pascual *et al.* 1996). Additional studies reviewed by Lewis (2003) shown that radiopacifiers may have a positive effect on the fatigue life of acrylic bone cement, although this depended on the particle size and morphology, with the inclusion of “nanoparticles” of BaSO_4 (~100 nm in diameter) leading to significant increases in the fatigue life (Ginebra *et al.* 2002). This improvement in fatigue life was attributed to crack tip blunting, possibly due to the increased number of BaSO_4 particles encountered by the crack tip. This is in agreement with Vallo *et al.* (1997) who proposed that it is the interactions between the crack front and secondary phase particles that account for an increase in toughness; such a mechanism would involve ‘crack

pinning' and, in effect, an increase in crack length. Conversely, detrimental effects on bending strength, bending modulus and impact strength have been reported after increasing the loading of radiopaque agents (Liu *et al.* 2001). These reductions have been linked to limited bonding between the BaSO₄ particles and the host polymeric matrix (Molino and Topoleski, 1996). Furthermore, it has been observed that large agglomerations of BaSO₄ can act as fatigue crack initiation sites with the potential of causing overall failure (Kurtz *et al.* 2005).

4.8 Micromechanical analysis of fatigue failure

When examining the fatigue life of PMMA bone cement, Topoleski *et al.* (1993) suggested that micro-crack propagation occurred primarily through the inter-bead matrix, in addition to micro-crack formation ahead of the crack tip, as is modeled in Figure 12. Topoleski *et al.* (1993) also stated that the PMMA beads themselves may experience cleavage or crazing during rapid fracture. Other works by Murphy and Prendergast (2002) suggested that micro-cracks propagate primarily through the inter-bead matrix, but indicated that crack arrest could occur within pre-polymerised beads.

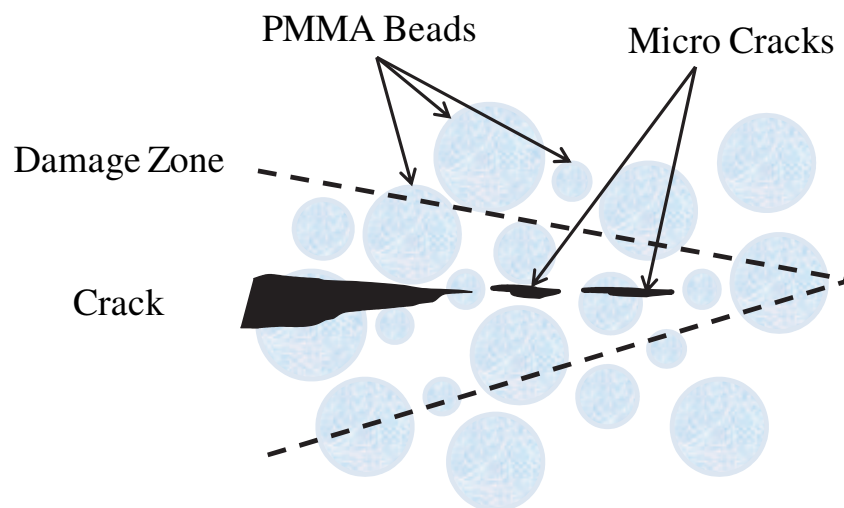


Fig. 12. Schematic of the proposed model of fatigue crack propagation and damage formation of Topoleski *et al.* (1993).

In relation to the porosity that remains after mixing, it is well established that the lower the porosity, the better the static and dynamic properties of cement (Dunne and Orr 2002). Murphy and Prendergast (2000/2002) suggested that pore initiated fractures may be linked to mechanical stress concentration, caused by adjacent PMMA beads at the pore surface, as seen in Figure 13. Topoleski *et al.* (1993) also suggested that pores situated within the fatigue crack damage zone act as micro-crack nucleation sites (see Figure 14), effectively increasing the area of the fatigue damage zone ahead of the crack tip. Conversely, the presence of porosity promotes levels of micro-crack initiation and could be considered to increase rates of crack propagation. Hence porosity can be seen as being both destructive and constructive. Finite element (FE) analysis showed that pores contributed to both fatigue crack acceleration and deceleration, depending on the location of the pores within the stress field, irrespective of size (Janssen *et al.* 2005a). Crack retardation was prominent when pores existed near to the propagating crack, but not close enough to initiate the crack deviating from its original

path. The presence of the pore in this scenario reduced the stress in the cement by causing the formation of secondary cracking initiating at the pore.

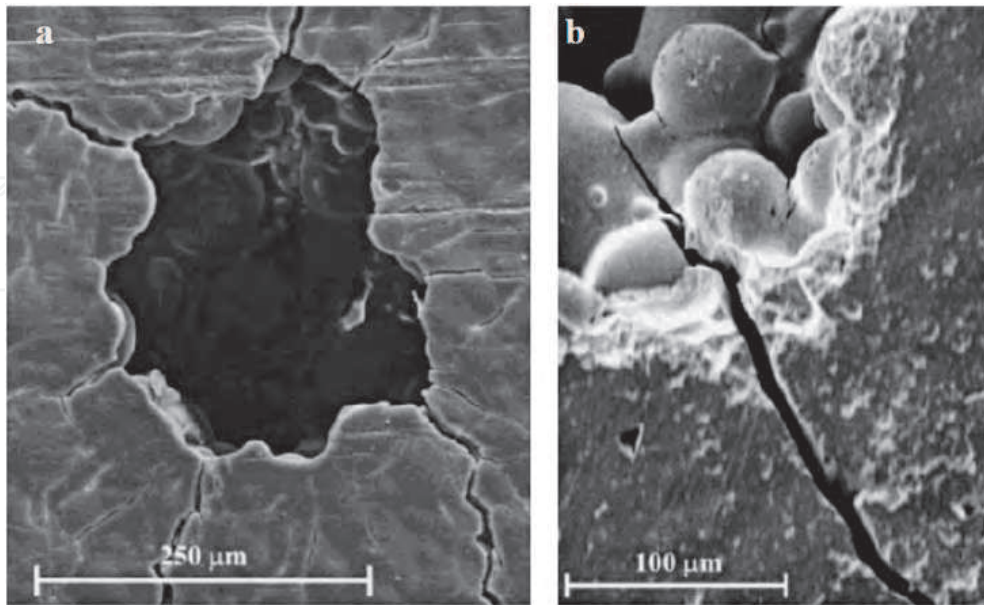


Fig. 13. SEM micrograph of (a) microcracks propagating from a pore and (b) a crack initiation site at a stress concentration between PMMA beads (Murphy and Prendergast 2002).

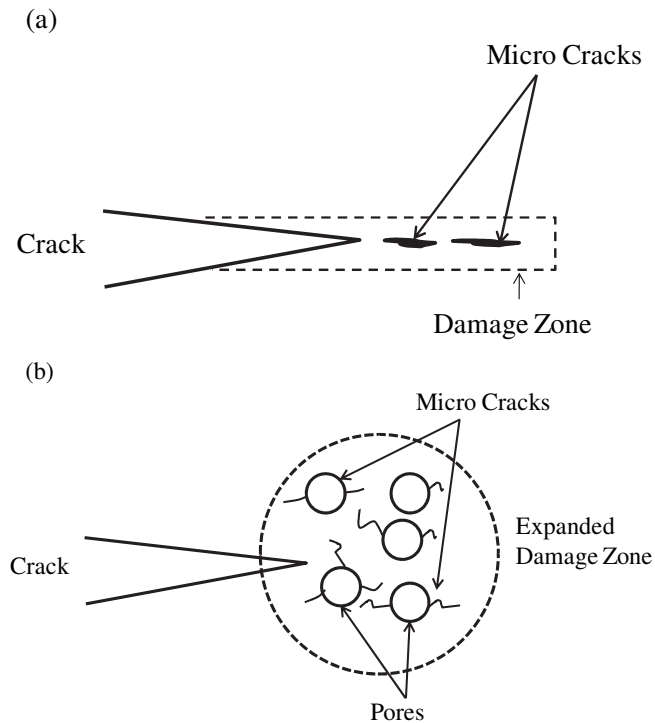


Fig. 14. Expansion of the fatigue crack due to porosity at the crack tip, as suggested by Topoleski *et al* (1993). (a) Damage zone remains linear when no pores are at the crack tip. (b) Expansion of damage zone as a result of micro-crack nucleation (i.e. pores).

In general, it is understood that crack propagation characteristics of bone cement at a microstructural level are heavily reliant on whether the failure regime is a fatigue crack or a fast 'impact' fracture (Prendergast 2001b). Fatigue crack propagation is directly influenced by bone cement microstructure, porosity, residual stresses and agglomerations of radiopaque agent. An impact or fast failure however, does not have a dependence on these same parameters. For any polymer, the success in achieving improved mechanical performance remains in the materials' potential to inhibit or delay crack initiation and improve its resistance to crack propagation.

5. Developments in acrylic bone cement

5.1 Mechanical properties

The intrinsic mechanical properties of acrylic bone cement (such as strength, fracture toughness and fatigue crack propagation resistance) in addition to the presence of extrinsic factors such as porosity, agglomerates of radiopaque agents and other such stress concentrations may limit its long-term survival (Lewis 2003). Within the current literature there have been many attempts to improve the fatigue performance of Acrylic bone cement. Most studies have tried to control the extrinsic factors, in particular porosity (Norman *et al.* 1995; Murphy and Prendergast 2000; Lewis 2003) by means of vacuum mixing or centrifugation. However, this does not address the underlying intrinsic factors which can be broadly categorised into two areas: (a) mechanical studies, focusing on improving mechanical performance, and (b) biological studies where the focus may be on the effect of bioactive inclusions or the addition of antibiotics.

5.2 Mechanical performance

A significant portion of the literature is directed towards discussing the potential to increase mechanical performance of acrylic bone cement *via* reinforcement with fibres or secondary phase particles: for example, carbon (Pilliar *et al.* 1976; Robinson *et al.* 1981; Pal and Saha 1982; Wright and Robinson 1982; Saha and Pal 1986), polyethylene (Yang *et al.* 1997; Narva *et al.* 2005), titanium (Topoleski *et al.* 1998; Kotha *et al.* 2006), hydroxyapatite (HA) (Serbetci *et al.* 2004), glass beads (Shinzato *et al.* 2000), glass flake (Franklin *et al.* 2005), glass fibres (Narva *et al.* 2005), and steel fibers (Kotha *et al.* 2004). Mechanical properties that have been reported to improve include: compressive, tensile, and bending strength, elastic modulus, fracture toughness and fatigue resistance, when compared to cement without reinforcement. In addition to the mechanical improvements provided by these fillers, further benefits have been identified with respect to the peak temperature reached during polymerisation. As mentioned previously, high temperatures experienced *in vivo* can cause thermal necrosis of the bone cells surrounding the cement mantle, in addition to the coagulation of blood, which can potentially lead to aseptic loosening of the implant, and ultimately implant failure (Lewis 1997). Reduced *in situ* polymerisation temperatures have been observed for, but not limited to, steel, carbon fibres (CF) and multiwalled carbon nanotube (MWCNT) reinforced bone cement (Pilliar *et al.* 1976; Saha and Pal 1986; Kotha *et al.* 2004, Marrs *et al.*, 2006). A number of researchers have investigated adding CF as a reinforcing agent using clinically applicable cement mixing techniques for both *in vitro* testing (Robinson *et al.* 1981; Pal and Saha 1982; Wright and Robinson 1982; Saha and Pal 1986;) and for *in vivo* applications (Pilliar *et al.* 1976). Pilliar *et al.* (1976) reported that the inclusion of randomly oriented CF (0.6 cm) improved fatigue performance, tensile strength, Young's modulus and impact

resistance (i.e. indicative of toughness), compared to cement without reinforcement. The thermal properties were also observed for the two cement types; the dough time and the setting time were unaffected by the addition of CF, whilst the maximum curing temperature was lowered for the cement with added CF (53 °C compared to 57 °C). Interestingly these research groups found that the addition of CF increased the viscosity of the cement above the required level by ASTM standards (ASTM F451-99a), meaning that use of these cements in a clinical setting would not be ideal. Fractographic analysis identified poor distribution of CF, and evidence of poor CF-PMMA bonding, although fibre pullout was noted. This CF-reinforced cement was used *in vivo* with no detrimental mechanical or biological response observed after 18 months. During the 1980s, problems associated with the high starting viscosity of the cement, and subsequent reduced levels of intrusion, were investigated *in vitro* following the development of low viscosity cement. Robinson *et al.* (1981) confirmed that CF-reinforcement of a commercial cement increased fracture toughness of both regular and low viscosity cements. However, the low viscosity cements (both reinforced and conventional) displayed a reduction in fracture toughness when compared to the equivalent regular viscosity cement. For the reinforced cement, Wright and Robinson (1982) reported a decreased crack growth rate versus the unreinforced cement). Saha and Pal (1986) investigated the effect of mechanically, or hand-mixed CF-reinforced bone cements, and found that mechanical mixing provided superior performance. They attributed this to the improved dispersion of CFs throughout the cement matrix.

Investigations concerning the addition of titanium (Topoleski *et al.* 1998; Kotha *et al.* 2006) or CF (Pilliar *et al.* 1976; Saha and Pal 1986) to bone cement suggested that commercially viable mixing methods are indeed possible. Topoleski *et al.* (1998) used SEM analysis to confirm that before cement failure, a good bond between the fibers and the host matrix existed, although subsequent damage led to evidence of fiber de-bonding, plastic deformation and ductile rupture of the fibers. Topoleski *et al.* (1998) also reported that the presence of the fibers prevented crack propagation (Topoleski *et al.* 1998). Additionally, fiber based additives have been shown to dissipate energy associated with static crack propagation, resulting in improved fracture toughness of acrylic bone cement, through crack diversion and crack tip blunting (Gilbert *et al.* 1995). Orientation and dispersion of the fibers, in addition to good interfacial bonding, were all identified to have a positive effect on improving mechanical properties due to reinforcement (Gilbert *et al.* 1995; Yang *et al.* 1997).

5.3 Biological performance

Bone cement is a biologically inert component of the implant construct. Conventional acrylic bone cement does not normally promote bone ingrowth. Several studies however have attempted to improve the biological performance of bone cement. These have included the incorporation of bioactive agents, such as HA based powders, glass ceramic particles or glass beads (Lee *et al.* 1997; Mousa *et al.* 2000; Shinzato *et al.* 2000). Each of these additives has been reported to enhance the biocompatibility of bone cement, thus reducing the formation of fibrous tissue at the bone-bone cement interface. Mousa *et al.* (2000) used apatite-wollastonite glass ceramic (AW-GC) particles to reduce the amount of monomer required for polymerisation, which lead to a reduction in the peak exotherm, and thermally induced bone necrosis as well as decreasing the levels of cement shrinkage. Similar results have been reported for cements containing glass beads, which have also been shown to improve bioactivity (i.e. osteoconductivity) compared with HA powder (Shinzato *et al.*

2000). Additionally, it has been reported that many of these bioactive cement composites exhibited no detrimental influence on mechanical performance, and in some cases improvements were observed (Mousa *et al.* 2000; Shinzato *et al.* 2000).

Concerns regarding biological performance include the use of antibiotics, which are integrated to reduce risk of infection and associated revision (Kuehn *et al.* 2005); many antibiotic-loaded cements are currently commercially available and, for those containing gentamicin sulphate, are believed to not cause any adverse affect on the fatigue performance (Baleani *et al.* 2003).

6. Polymer matrix composites

The mechanical success of any polymer composite is governed by the successful transfer of load between the matrix and the reinforcement. This transfer of load is dependent upon the volume fraction, dispersion, orientation of the reinforcing phase, the host matrix-reinforcement interface and the individual mechanical properties of the phases that are present (Gilbert *et al.* 1995; Hull and Clyne 1996b; Yang *et al.* 1997). Within fibre-reinforced composites four main microstructural regions exist: (1) the matrix, (2) the fibre, (3) the interface, and, in some composite systems, (4) the interphase. An interphase may be present if a mechanical or chemical interaction takes place between the polymer matrix and the reinforcing phase (examples includes adsorption of the polymer onto the surface of the reinforcing agent in particulate-reinforced polymers, inter-diffusion of the components during blending and chemical reactions at the polymer/fibre interface) (Pukanszky 2005).

Fibres aligned in the direction of applied load are particularly effective at reinforcing composites. Corresponding mechanical properties which effect failure performance may be identified, with a complex interaction between individual phase properties, the interface strength between the host polymer and the reinforcing fibres and the composite microstructure. Polymers are the most common form of composite matrix and are often reinforced with a low fraction of fillers such as glass, CF or Aramid. This results in composites of high specific strength and modulus as the low levels of additives allows a more homogeneous dispersion (Callister 2000a). Of these three reinforcements, CF composites often exhibit the best resistance to fatigue failure due to superior mechanical properties as well as the higher thermal conductivity of carbon fibres which assists in the dissipation of heat during cyclic loading (Scheirs 2000a). In compression, the mechanical performance of fibre-reinforced composites is dependent on the interaction between the host polymer matrix and the fibre. For optimum reinforcement, the matrix would provide lateral stabilisation to the fibre preventing subsequent buckling. Alternatively, the tensile behaviour is governed by the tensile strength of the fibre additive (Hull and Clyne 1996a). Fatigue failure in polymer composites is commonly characterised by a gradual reduction in stiffness (Scheirs 2000c). Without reinforcement, fatigue failure typically occurs perpendicular to the applied load; in contrast, the presence of fibres generally results in a diffuse damage zone due to the combination of a number of sub-critical failure modes and crack shielding mechanisms. In general, crack propagation through fibre-reinforced polymers may be considered as a multi-faceted interaction between the polymer matrix, the fibre reinforcement and the associated interface/interphase regions. A combination of mechanisms may occur and subsequently, fibre inclusions may impede crack growth by three main mechanisms (Mandell *et al.* 1980; Sauer and Richardson 1980):

- i. Debonding of interface/interphase between fibre and matrix – as a crack approaches, failure of the interface occur serving to blunt the crack tip and reduce crack propagation.
- ii. Crack bridging – transferring load across a given matrix crack, reducing the crack.
- iii. Fibre pullout, subsequent to crack bridging, may also absorb energy due to matrix deformation and/or interface friction.

7. Carbon nanotubes

It was in 1980 that Sumio Iijima first recorded an ‘onion-shaped particle’ in the order of 0.8 – 1 nm in diameter. It was not until five years later that Iijima realised that this ‘onion-like structure’ was the fullerene C₆₀, which was believed to be discovered by Kroto, Heath, O’Brien, Curl and Smalley in 1985, (Figure 15).

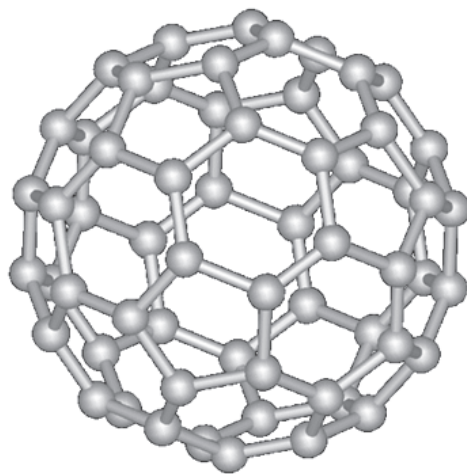


Fig. 15. Carbon C₆₀ molecule (Iijima, 1991).

Although Curl *et al.* (2001) later confirmed that it was Osawa who first documented the concept in 1970. It was in 1991, whilst working as an electron microscopist that Iijima’s study of soot deposited on the cathode during the arc-evaporation synthesis of fullerenes led to the sighting of a needle-shaped material. What was originally described as “*microtubules of graphitic carbon*” is now commonly known as carbon nanotube (CNT). Whilst being considered an accidental discovery, Iijima believes it was the “*power of serendipity*”. Initially, Iijima produced individual tubes of graphitic carbon with diameters of 4-30 nm and a length of up to 1 μm using arc-discharge evaporation methods (Iijima 1991). At present, CNT can be synthesised *via* electric arc discharge (Iijima 1991; Shi *et al.* 2000), laser ablation (Zhang *et al.* 1998; Zhang and Iijima 1998) or, more commonly chemical vapour deposition (Sinnott *et al.* 1999; Andrews *et al.* 2002). Extensive research has been conducted on these processing methods by Andrews *et al.* (2002), and Thostenson *et al.* (2001).

CNT can occur as either single-walled nanotube (SWCNT) or multiwalled nanotube (MWCNT) structures. SWCNT consist of a single graphene sheet rolled up as a seam-free tube. They can be thought of as a linearly extended fullerene (Ajayan 1997; Iijima 1991/2002; Baughman *et al.* 2002). SWCNT usually exist as agglomerations due to the van der Waals forces between each tube, with diameters on average between 0.7-2 nm, whilst their lengths are often 5-30 μm (Ajayan 1997; Colbert 2003). MWCNT can be described as an array of

SWCNT that are concentrically arranged inside one another with an internal diameter as small as 2.2 nm. The distance between the individual SWCNT that constitute MWCNT (or the graphite inter-layer separation) is typically 0.34 nm (Ajayan 1997; Iijima 1991/2002) (Figure 16). Iijima (1991) used electron diffraction to establish that the crystal axis of the graphene tubes consisted of carbon-atom hexagons arranged in a helical manner about the tube axis (Figure 17). The ends of CNT are closed off by the presence of pentagonal carbon rings near the tip regions, whilst deformations and imperfections of the cylinder occur as pentagons or heptagons within the main structure of the tube (Ajayan 1997).

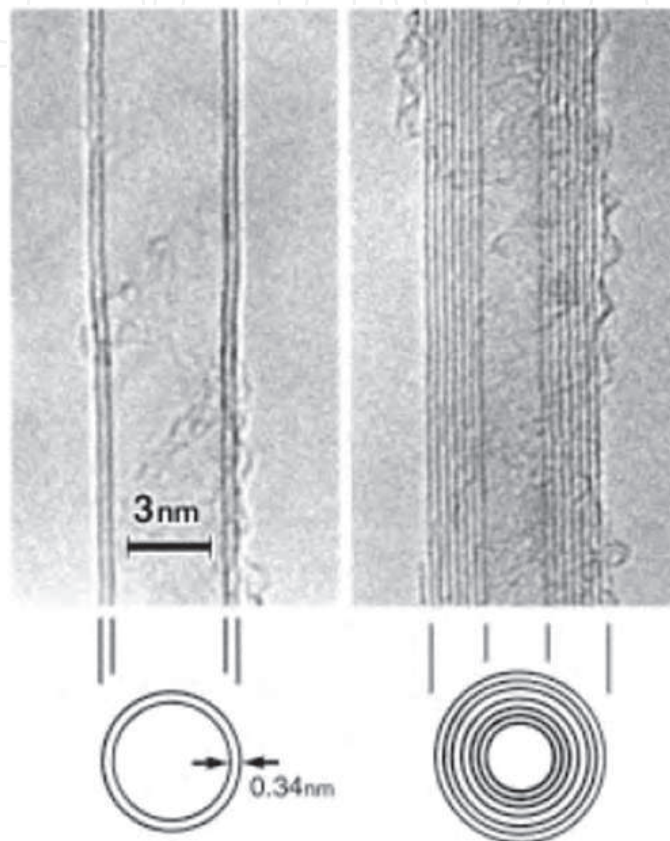


Fig. 16. Transmission electron micrograph (TEM) of MWCNT (Iijima 1991).

SWCNT, are known to be stiff and exceptionally strong (high Young's modulus and high tensile strength). Furthermore, SWCNT can stretch beyond 20% of their original length and bend over double without kinking (Baughman *et al.* 2002; Colbert 2003). However, the mechanical properties of individual CNT, whether SWCNT or MWCNT are the subject of much research with a significant variation in recorded properties existing. The use of CNT in various matrices can greatly enhance mechanical properties. Wong *et al.* (1997) provided an insight into the potential uses of CNT. Atomic force microscopy (AFM) was employed to determine the elasticity, strength and toughness of individual silicon carbide nanorods (SiC NRs) and MWCNT that were attached to molybdenum disulphide surfaces. The average bending strength of the MWCNT was 14.2 ± 8.0 GPa; with the maximum bending strength being substantially smaller than that of the SiC NRs at 53.4 GPa. In contrast, whilst both nanostructures exhibited high values for the Young's modulus (highlighting their suitability as reinforcing agents in ceramic, metal and polymer matrix composites) the Young's modulus for

the MWCNT was almost double that of the SiC NRs (1.28 ± 0.59 TPa and ~ 600 GPa, respectively). The Young's modulus value for the in-plane modulus of highly orientated pyrolytic graphite was recorded at 1.06 TPa (Blakslee *et al.* 1970) and is believed to be the largest known for a bulk material. Wong *et al.* (1997) concluded that while the stiffer MWCNT had a lower ultimate strength, the elastic buckling displayed by the MWCNT (i.e. the energy storing capabilities of CNT before failure) showed them to be the "tougher" nanostructure. More recently, Demczyk *et al.* (2002) investigated the direct failure of individual MWCNT under tension using TEM. While the mode of failure, either ductile or brittle, could not be determined, results confirmed a tendency to fail *via* a mode now known as 'telescopic failure', with initial failure observed in the outermost walls followed by a 'sword in sheath effect' of the inner cylinders. TEM observations also confirmed the elastic capabilities of MWCNT during deformation in bending, even after being highly distorted.

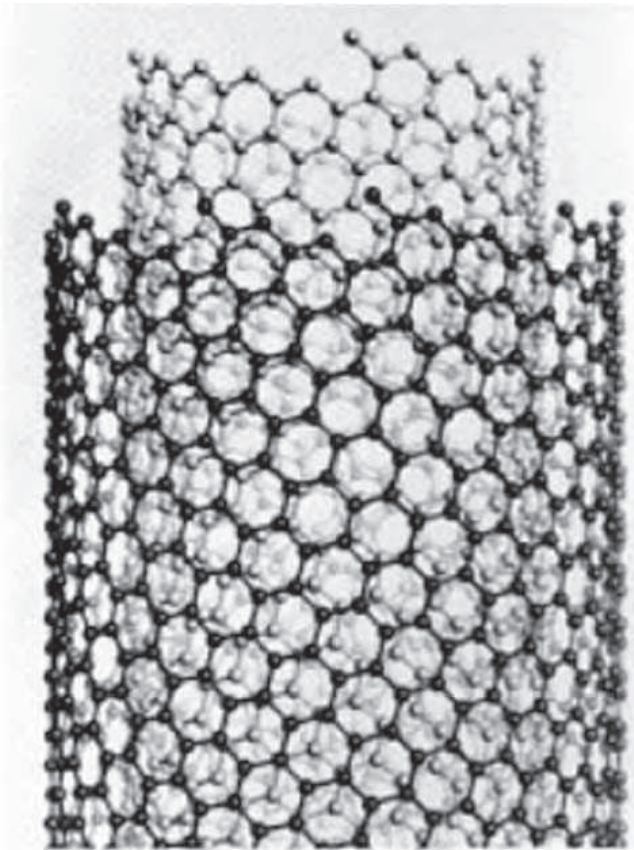


Fig. 17. Helical arrangement of carbon atom hexagons that make up a graphene sheet in a MWCNT (Iijima 1991).

It is clear that CNT offer significant potential to improve the properties for many existing materials; the challenge remains for the superior properties exhibited by CNT individually to be successfully applied and optimised in practical applications such as nanocomposites. Not only do the properties of the CNT themselves vary due to impurities during processing (Baughman *et al.* 2002), but on addition of CNT to a matrix, the problem becomes multi-faceted: CNT dimensions, dispersion, alignment, concentration, CNT-matrix interface/adhesion and choice of matrix are some of the many issues that govern the final properties of the composite material. At present, production of high purity SWCNT still

remains costly and of a low yield: purification reduces yield further, adds to cost and damages the structure (Andrews *et al.* 2002). Low manufacturing costs and high yields of aligned MWCNT are now possible however, making them the preferred choice in bulk composite material development.

8. Properties of CNT-reinforced polymers

Since the discovery of CNT in 1991, research incorporating them into various matrix materials has been plentiful. This increase in research can be attributed to the fact that CNT have extremely high aspect ratios (typically >150:1), modulus and low density. The addition of CNT to polymer composite materials has enhanced mechanical (Wong *et al.* 1997; Andrews *et al.* 2002), electrical (Baughman *et al.* 2002; Colbert 2003) and thermal properties (Kim *et al.* 2001; Baughman *et al.* 2002; Colbert 2003), in matrices including polycarbonate (Ding *et al.* 2003; Eitan *et al.* 2006), polystyrene (Andrews *et al.* 2002; Thostenson and Chou 2003; Park *et al.* 2005) ultrahigh molecular weight polyethylene (Ruan *et al.* 2003) and PMMA (Hwang *et al.* 2004; Marrs *et al.* 2005).

Extensive literature has explored the effects of CNT on mechanical properties of various polymer matrices. It has been shown that the addition of CNT can increase the toughness of polymer matrices due to crack bridging, changes in morphology of the matrix and the additional energy required for de-bonding and nanotube pullout (Dalton *et al.* 2003; Ruan *et al.* 2003; Andrews and Weisenberger 2004). As with other polymer composites, increases in modulus may be identified with stress transfer from the matrix to the CNT. It should be noted though that the presence of agglomerations of CNT can have significant adverse influence on the mechanical properties of CNT-polymers, acting as stress concentrations and fracture initiation points within the composite microstructure. This effect was recorded by Marrs *et al.* (2005), who incorporated MWCNT at various levels of loading in to PMMA bone cement. They characterised the fatigue, quasi-static tensile and bend properties for these MWCNT-PMMA nanocomposites. They found that the optimal performance was for the addition of 2 wt% MWCNT. They also report that loadings above this resulted in reduced mechanical properties, although results were still superior when compared to pure PMMA (Marrs *et al.* 2005). Cadek *et al.* (2004) reported an increase in Young's modulus by a factor of two after the addition of 0.6 vol% CNT to poly (vinyl alcohol), an effect which they attributed to nanotube diameter and resultant surface area. Varying levels of reinforcement as a result of a change in nanotube diameter suggested that MWCNT of smaller diameter provided optimal reinforcement due to increased surface area. Whilst the enhancing effects of CNT with respect to tensile strength and modulus have been recorded (Ruan *et al.* 2003), it has been established that theoretical predictive models such as Rule of Mixtures approach or the Halpin-Tsai model predict superior reinforcement capabilities than experimental data provides. Part of this discrepancy may be due to factors such as poor interfacial bonding, inhomogeneous dispersion, and CNT quality (Andrews *et al.* 2002; Fisher *et al.* 2002; Andrews and Weisenberger 2004). Poor adhesion/bonding at the interface between the host polymer and the CNT may have a detrimental effect on the mechanical properties of CNT-composites (Andrews *et al.* 2002). Nanotube pullout experiments, using atomic force microscopy, may be used to determine the force required to separate a single CNT from a polymer matrix (Barber *et al.* 2003; Baroud *et al.* 2004). It is widely accepted that a strong interfacial adhesion between the reinforcing nanotube and the polymer matrix leads to the effective transfer of load (Cooper *et al.* 2002; Barber *et al.* 2003; Goh *et al.* 2003, Marrs *et al.*,

2007). Barber *et al.* (2003) measured the average interfacial stress required to remove a single MWCNT from a polyethylene-butene matrix as 47 MPa. Comparing this value to the 10 MPa measured for poorly bonded interfaces in other fibre-reinforced polymers, Barber *et al.* (2003) suggested that this enhancement was due to the presence of covalent bonding at the interface between CNT and the host polymer, potentially due to a chemical interaction between the polyethylene-butene matrix and defects on the surface of the nanotube. Moreover, it is believed that the mechanical properties of the polymer immediately surrounding the nanotube may be enhanced when compared to the bulk of the polymer. Nano pullout test results by Barber *et al.* (2003) showed no evidence of the polymer yielding, even at pullout stresses that were ten times higher than average tensile strength of the polymer matrix. This may be explained using differential scanning calorimetry (DSC) measurements to determine the polymer crystallinity. Cadek *et al.* (2004) compared polymer crystallinity for PVA after the addition of 0.6 vol. % CNT and measured a linear increase in crystallinity with increasing volume fraction of CNT, suggesting a crystalline polymer coating is formed at the nanotube surface. Observations of the fracture surface using SEM confirmed that polymer wetting of the nanotube surface was achieved (Figure 18); diameters of the nanotubes in the composite were larger than the as-received CNT (Ding *et al.* 2003).

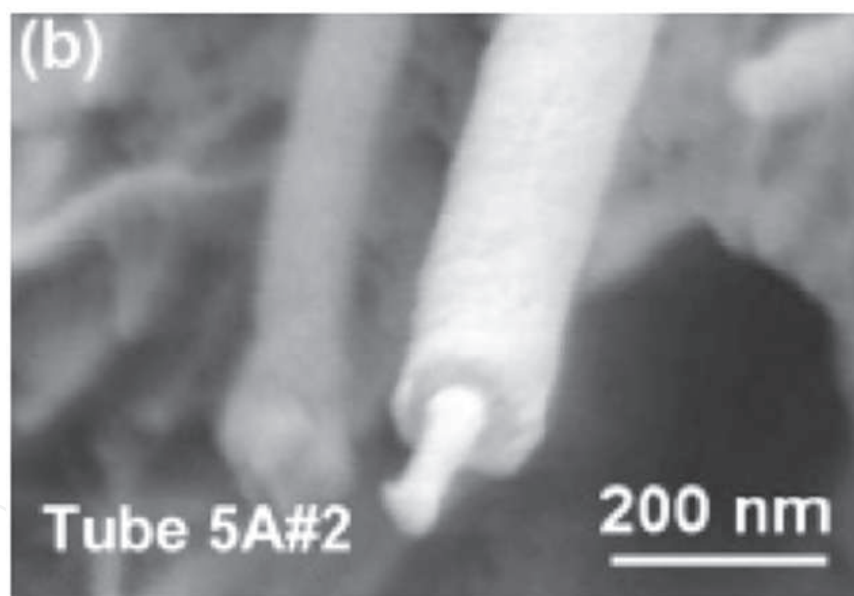


Fig. 18. High-resolution SEM image highlighting MWCNT coated with a polymer sheath protruding from a MWCNT-polycarbonate fracture surface, as observed by Ding *et al.* (2003).

The interface between the host matrix and reinforcement phase, in addition to the interphase region may play a pivotal role in optimising the mechanical performance of a polymer composite (Gilbert *et al.* 1995; Hull and Clyne 1996b; Yang *et al.* 1997; Eitan *et al.* 2006). When investigating the effect of MWCNT on the crystallinity of PVA and PVA nanocomposites Ryan *et al.* (2006) used dynamic mechanical analysis (DMA) to confirm significant improvements in the Young's modulus. Ryan *et al.* (2006) also confirm the findings reported by Marrs *et al.* (2005), reporting that limits in the amount of CNT added to

the polymer exist for achieving optimal mechanical performance. Ryan *et al.* (2006) explained that improvements in mechanical properties are seen for lower fractions of CNT with detrimental effects introduced at higher levels of loadings due to the higher incidence of CNT agglomerations. Of further interest is the degree of crystallinity present at the CNT-polymer interface: reported for CNT-reinforced PVA, the large increases in Young's modulus were attributed to the variations in crystallinity. A consequence of the ability of CNT to act as nucleation sites for crystals in both the solution and melt/solid-state phase (Coleman *et al.* 2004; Ryan *et al.* 2006). It is the presence of a well-bonded crystalline interface between the polymer matrix and the nanotubes that may account for the improved mechanical properties due to the increased levels of stress transfer (Cadek *et al.* 2004; Coleman *et al.* 2004). This would allow for failure/crack deflection to occur at the matrix-crystalline interface rather than at the nanotube interface. It has been highlighted that the presence of CNT agglomerations, particularly seen with the use of SWCNT, limits the ability of PVA to act as crystal nucleation sites and, as a result inferior mechanical performance are not seen. Similar findings have been reported for other semi-crystalline polymers (Hull and Clyne 1996a) such as UHMWPE (Ruan *et al.* 2003), polypropylene (Leelapornpisit *et al.* 2005; Seo *et al.* 2005) and polyamide (Chao *et al.* 2006). These reports highlighted the need for careful selection of the processing method that allows for optimal levels of crystallisation at the nanotube-matrix interface (Coleman *et al.* 2004). To date, limited work has been published regarding the crystallisation of PMMA at the nanotube-matrix interface: Coleman *et al.* (1998) proposed that PMMA would be unable to bond to CNT due to the spatial arrangement of the polymer. Alternative mechanisms have been sought to improve the interface and interphase properties of CNT- amorphous polymers. The most commonly employed approach is the covalent attachment of chemically functional groups to the CNT at the defect sites. This is completed in order to achieve similar polymer sheathing effects around the nanotube. In chlorinated polypropylene, Coleman *et al.* (2004) reported that the thickness of the polymer sheath surrounding the nanotubes depends on the volume occupied by the functional groups. Upon failure, fracture was seen to occur away from the CNT-polymer matrix interface. Immobilisation of the polymer chains in the region surrounding the nanotubes was proposed as an additional reinforcement mechanism associated with MWCNT-reinforcement of amorphous polycarbonate. Functionalisation of the MWCNT surface led to an increase in thickness of this interphase region, subsequently improving load transfer capabilities between the matrix and the nanotubes (Eitan *et al.* 2006). This suggestion was highlighted by Jia *et al.* (1999), they reported that PMMA can bond with CNT, although this was dependent on the processing methods utilised. Using *in situ* polymerisation, initiated using the free radical initiator, Azobisisobutyronitrile (AIBN), to form the polymer, additions of MWCNT (both unfunctionalised and carboxyl functionalised) resulted in nanocomposites of improved mechanical properties (in particular, tensile strength, toughness and hardness), with the carboxyl functionalised nanotubes out-performing their unfunctionalised counterparts. High interfacial strengths were associated with bonding between the open π -bonds of the CNT (believed to be initiated by the AIBN) and the open bonds in the PMMA possibly creating a C-C bond between the PMMA and the CNT. Jia *et al.* (1999) also reported that higher loadings of MWCNT led to a more brittle polymer with reduced toughness and tensile strength. Velasco-Santos *et al.* (2003) demonstrated the use of an amorphous polymer matrix is potentially advantageous over semi-crystalline polymers like PVA; clear reasoning behind

this is not given although the presence and nature of the interphase region may be an explanation.

9. Mechanisms of failure of CNT-polymers

Andrews *et al.* (2002) reported that CNT within polymer matrices under tensile stress may align themselves parallel to the direction of the applied load, enabling crack bridging behind a crack tip. Andrews *et al.* (2002) explained that this phenomenon reduced the stress concentration in the region surrounding the crack tip, and ultimately reduced crack propagation. Key reinforcement mechanisms that have been identified in CNT-polymer systems are nanotube pullout, bending of nanotubes (often due to surface defects such as iron oxide catalyst inclusions from the CNT production process) and telescopic fracture of nanotubes (Andrews *et al.* 2002; Cooper *et al.* 2002; Demczyk *et al.* 2002; Ding *et al.* 2003; Hwang *et al.* 2004). Such phenomena are schematically illustrated in Figure 19.

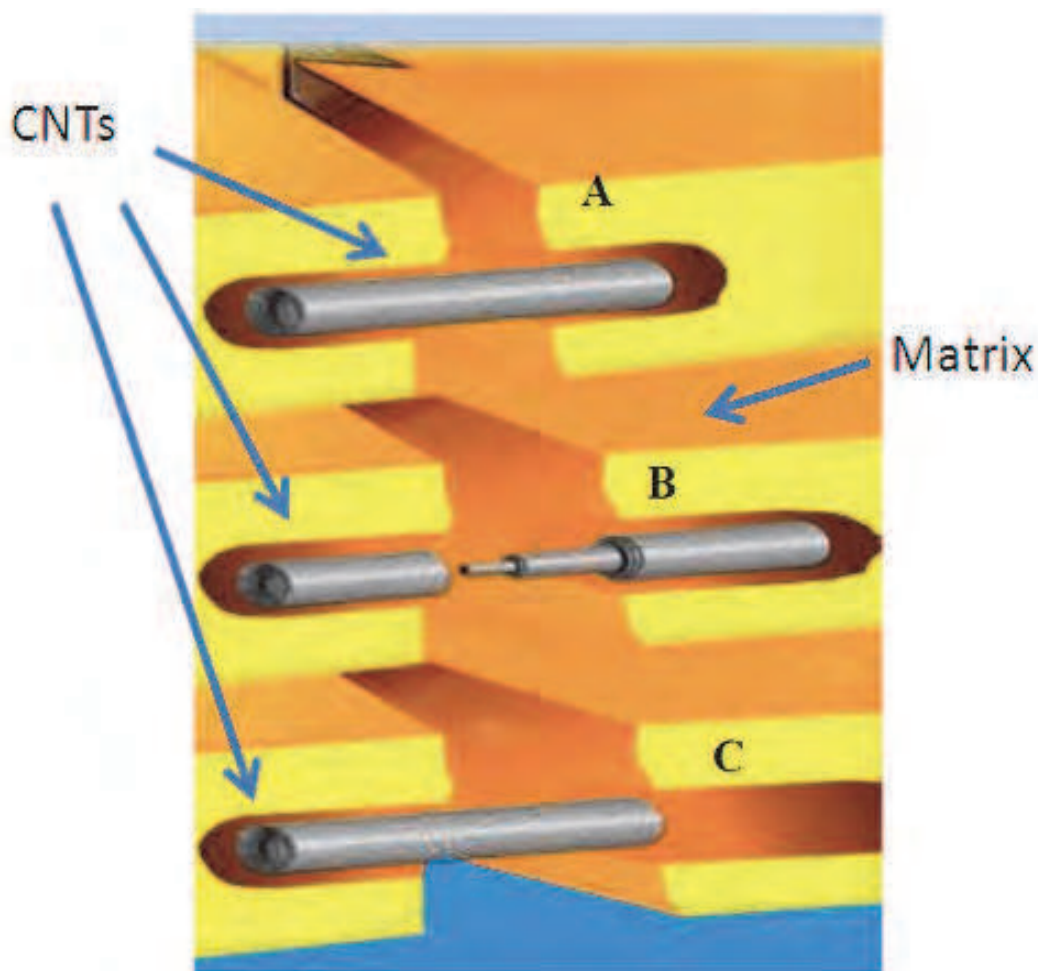


Fig. 19. Schematic illustration of (A) a CNT bridging a crack, (B) telescopic failure of a CNT and (C) CNT fibre pullout experienced in CNT-reinforced polymers (Sinnott and Andrews 2001).

Crack bridging of the matrix may arise in CNT-containing polymers. Hwang *et al.* (2004) directly observed nanotube pullout. (Figure 20b) and failure of the graphene layers resulting in telescopic failure (Figure 20c).

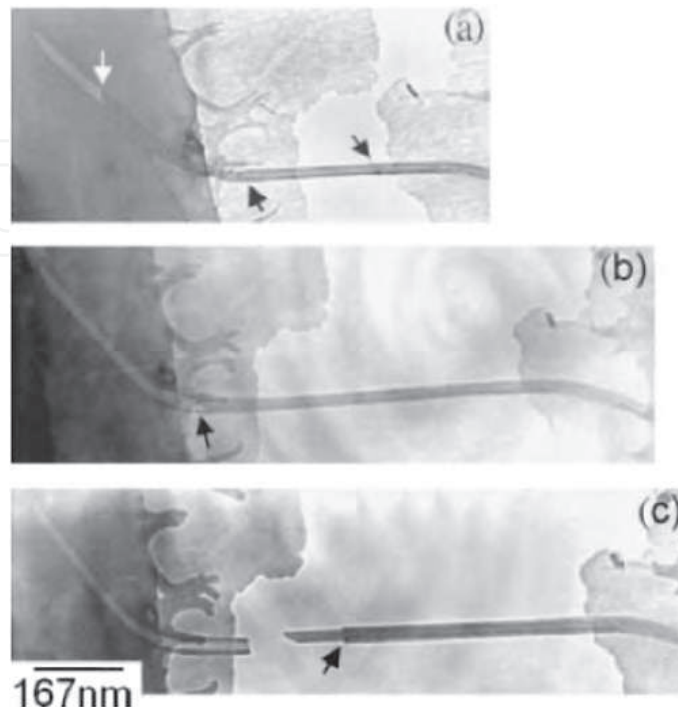


Fig. 20. TEM images of MWCNT-containing PMMA showing (a) breaking of graphene layers, (b) MWCNT pullout and (c) final telescopic failure of the MWCNT (Hwang *et al.* 2004).

10. Biocompatibility of CNT

The Royal Society and the Royal Academy of Engineering, UK, published a report (2004) discussing the associated ethical, health and safety, and social implications of nanotechnology (The Royal Society and the Royal Academy of Engineering 2004). With an increased interest in the use of nanotechnology, the Government later published its own report (*'Characterising the potential risks posed by engineered nanoparticles'*, November 2005) and follow-up studies (*'First quarterly update on the Voluntary Reporting Scheme for engineered nano-scale materials'*, December 2006). The full report addressed many issues concerning the potential use of nanotechnology and CNT. Concerns have been raised that the properties that promote the use of nanoparticles in certain applications may also have health implications, such as their high aspect ratios, surface reactivity and their ability to cross cell membranes (The Royal Society and the Royal Academy of Engineering 2004; Kagan *et al.*, 2005; Fadeel *et al.*, 2007). The report highlighted that the main risks associated with CNT stem from their high surface to volume ratio to which a target organ may be exposed, in addition to the chemical reactivity of the surface, the physical dimensions of the nanoparticles and their solubility. Speculation surrounding the use of CNT has equated their effect on health to that of asbestos (due to their similar size and shape). CNT are therefore suspected as being potentially carcinogenic, and additionally, may cause inflammation or functional changes to proteins due to their large surface area. However, it has been argued that no new risks to health have been introduced as a result of the increasing use of nanoparticles as part of composite materials, and that most concerns derive

from the possibility of detached, or 'free' nanoparticles and nanotubes from the matrix (The Royal Society and the Royal Academy of Engineering 2004). It is believed that, if airborne, the likelihood of CNT existing as individual fibres is improbable as electrostatic forces cause the CNT to agglomerate which reduces their ability to be inhaled into the deeper areas of the lungs. However, when investigating of the inhalation of stable non-purified SWCNT aerosols in mice, Shvedova *et al.* (2008) reported that the chain of pathological events was realised through an early inflammatory response and oxidative stress culminated in the development of multifocal granulomatous pneumonia and interstitial fibrosis (Figure 21).

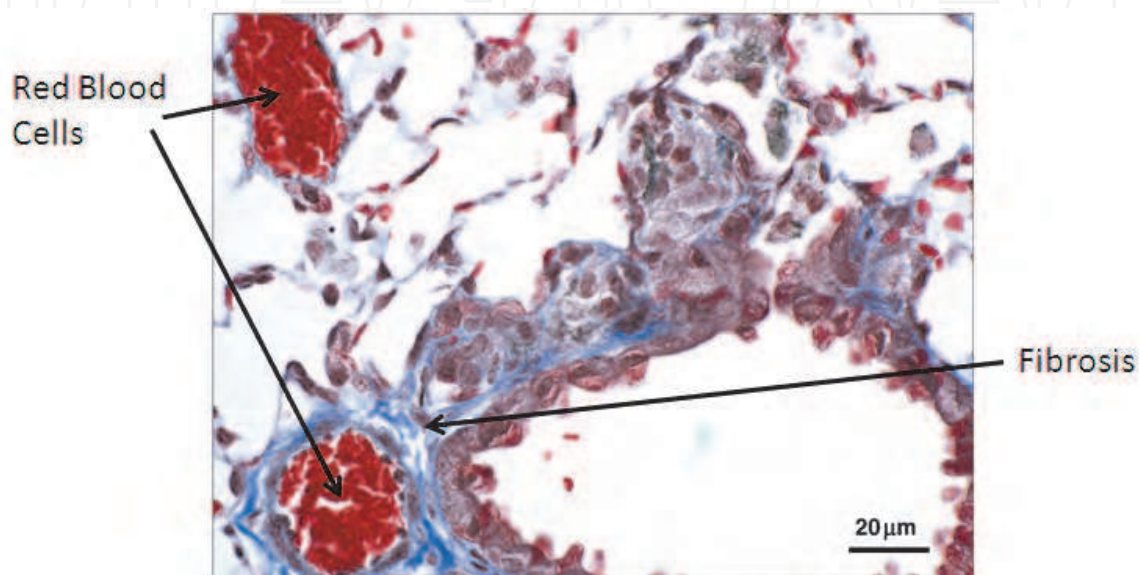


Fig. 21. Representative image of lung section from the SWCNT inhalation study depicting granuloma formation on day 28 post treatment. Fibrosis is indicated by blue staining in this Masson's Trichrome stained section of the lung (Shvedova *et al.* 2008).

Smart *et al.* (2006) reviewed the often conflicting findings pertaining to the cytotoxicity and biocompatibility of CNT. They concluded that, as-received (i.e. untreated, or unfunctionalised) CNT exhibited some degree of toxicity (observed both *in vitro* and *in vivo*) with detrimental effects associated with the presence of transition metal ions, used as catalysts in the CNT production. Smart *et al.* (2006) also reported that CNT that have been chemically functionalised have yet to demonstrate toxicity effects. It is highlighted that the tendency for CNT to aggregate may impact the reported results, although quantification of this fact has yet to be investigated. With research into the use of CNT, and nanotechnology ever increasing, the uncertainty regarding toxicity has been brought to public attention. As a result, it has been recommended that further research is necessary regarding the biological impacts of nanoparticles and nanotubes, including their exposure pathways within the body, and that methodologies for *in situ* monitoring should also be developed (The Royal Society and the Royal Academy of Engineering 2004). Recent studies have addressed the issue of CNT uptake by different cell types. While the results seem to be controversial, it is apparent that the presence or absence of specialised signals determined the recognition and subsequent interactions of CNT with cells. Overall, pristine CNT carrying no recognisable signals were poorly taken-up whereas CNT modified chemically (e.g. oxidatively modified and functionalised) or by adsorbed macromolecules (e.g. proteins, lipids) were more readily recognised and engulfed by cells (Shvedova *et al.*, 2010). Several *in vitro* studies support the

concept that pristine CNT are not readily taken up by lung cells. Davoren *et al.* (2007) reported no measurable uptake of CNT in A549 cells (a human alveolar type II cancer cell line). Likewise, Herzog *et al.* (2007) reported no uptake of CNT in either A549 cells or BEAS-2B cells (a human bronchial epithelial cell line). Lastly, no evidence of uptake of CNT was reported after electron microscopic evaluation of exposed RAW 264.7 cells (mouse peritoneal macrophage cell line) (Shvedova *et al.*, 2005). In contrast, functionalisation of SWCNT with a phospholipid signal, phosphatidylserine, made CNT recognisable *in vitro* by different phagocytic cells, including murine RAW264.7 macrophages, primary monocyte-derived human macrophages and dendritic cells, and microglia from rat brain (Figure 22) (Shvedova *et al.*, 2009).

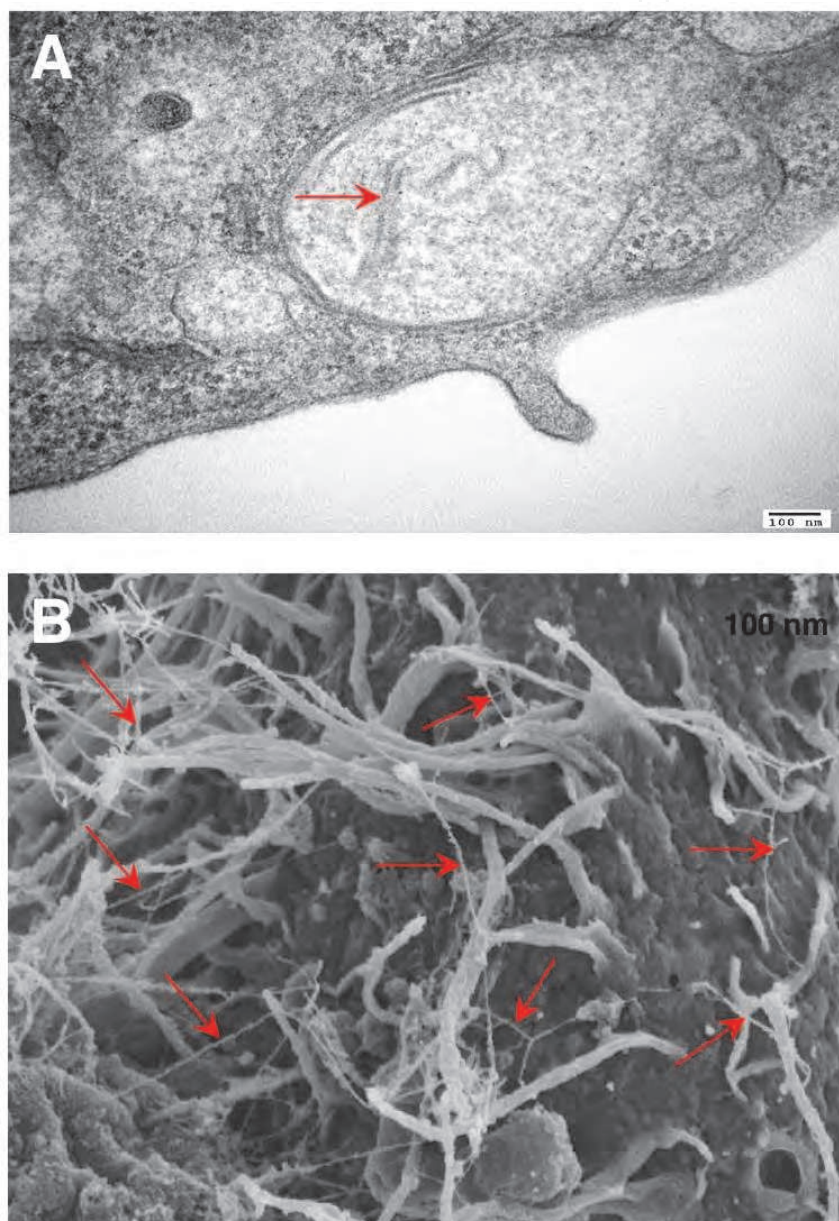


Fig. 22. Representative transmission electron micrograph (A) and scanning electron micrograph (B) of RAW264.7 macrophages with engulfed PS-coated SWCNT. Arrows indicate SWCNT. (Shvedova *et al.*, 2009).

11. CNT-reinforced biomaterials

Nanotechnology in biomaterials is not a new idea (Hrkach *et al.*, 1997). Nanomaterials have been used as implant coatings, bulk materials, drug delivery, actuators, diagnostic tools and devices (Sinha and Yeow, 2005). When biomaterials incorporating nanomaterials are studied, much of the emphasis is on the interaction between the biological tissue and the biomaterial at a molecular level. Using the interface between bone, and a metallic implant as an example, a positive biological interaction is essential if a good fixation is to be obtained. Chun *et al.* (2004) examined this interaction by coating titanium (Ti) substrates with helical rosette self-assembled organic nanotubes (HRN). HRN display chemical and structural similarities to various constituents of bone (Figure 23). Chun *et al.* (2004) found that the HRN-coated titanium displayed enhanced interaction with the naturally-occurring nanostructures' constituents such as collagen fibres and HA; this was measured as a function of the cell adhesion of human fetal osteoblasts (hFoBs) cells (Figure 24).

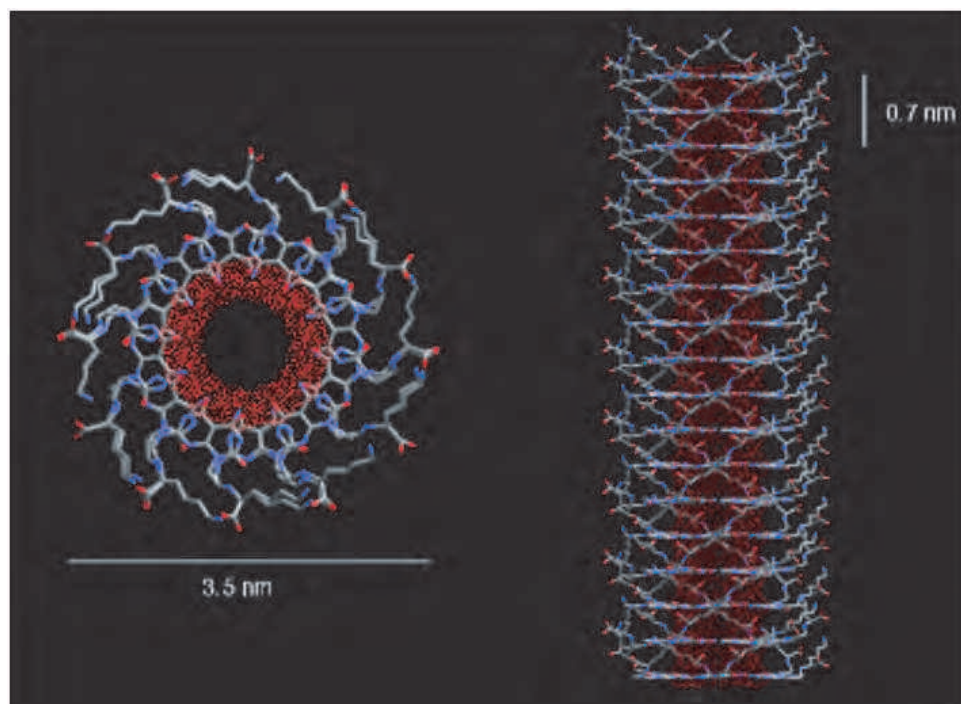


Fig. 23. Diagram of helical rosette nanotube (HRN) (Chun *et al.*, 2004).

Webster *et al.* (2004) incorporated carbon nanofibres (CNF) into polycarbonate-urethane (PCU) for neural or orthopaedic prosthetic devices. They reported that this material had the potential to increase neural and osteoblast functions, as cell attachment increased with CNF loading. Additionally they stated that the functions of cells that contributed to glial scar-tissue formation for neural prostheses (astrocytes) and fibrous-tissue encapsulation for bone implants (fibroblasts) decreased on the PCU composites containing increasing amounts of CNFs. In this manner, this study provided the first evidence that CNF formulations may interact with neural and bone cells, which is important for the design of successful neural probes and orthopaedic implants. Furthermore, Webster *et al.* (2004) summarised that using nanotechnology in biological systems may be potentially feasible as biological systems are governed by molecular behaviour at the nanoscale, and therefore the properties of which are accustomed to high levels of interaction at this nanoscale. This study by Webster *et al.*

highlighted the potential for CNT to be used in PMMA bone cement to encourage cell growth at the bone-cement interface with the aim of reducing aseptic loosening by enhancing the mechanical interlock in the cancellous bone.

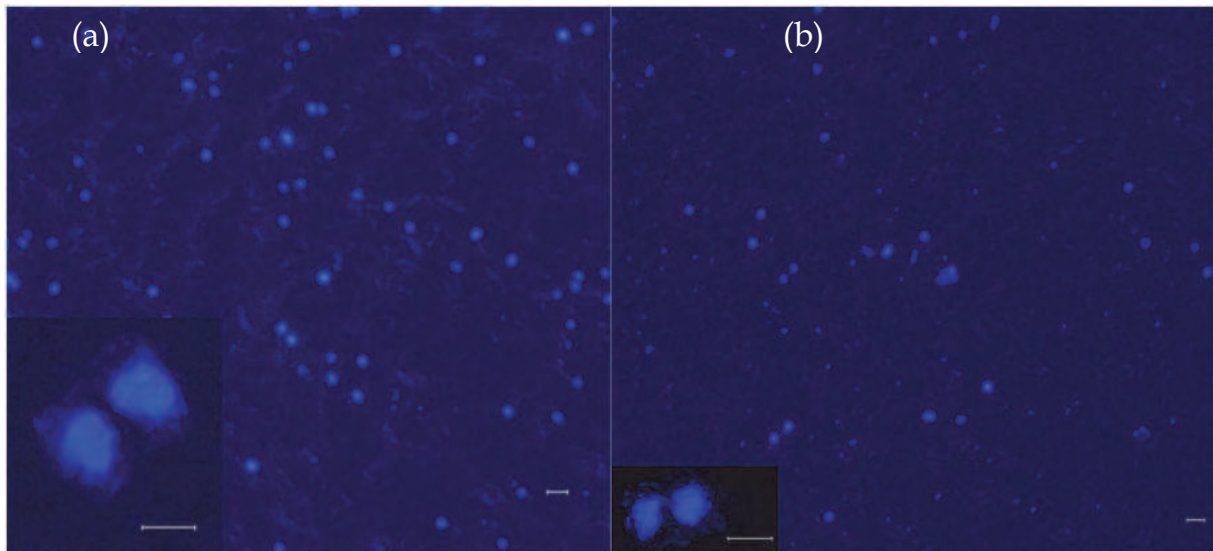


Fig. 24. Fluorescently stained cells on Ti substrates. (a) HRN coated Ti. (b) Uncoated Ti. (Magnification: 20 \times ; inset magnification 200 \times). Scale bars = 60 μm , inset bars = 50 and 100 μm for (a) and (b), respectively (Chun *et al.*, 2004).

CNT exhibit many unique mechanical, thermal, and electrical properties. However, their potential use for bioengineering applications and medical materials is almost wholly dependent on their biocompatibility. Cui *et al.* (2005) investigated the effect of SWCNT on human HEK293 cells (human embryo kidney cells). Results showed that SWCNT can inhibit HEK293 cell proliferation, inducing cell apoptosis (programmed cell death as controlled by the nuclei in normally functioning cells) and decreasing cellular adhesive ability in a dose and time-dependent manner. Their results also showed that HEK293 cells initiated active responses such as secretion of small 'isolation' proteins to isolate the cells attached to the SWCNT from the rest of the cell mass; a response that offers potential for medical chemistry and disease therapy.

Synthetic bone scaffolds is an area where the biocompatibility of materials used, such as polymers or peptide fibers, is still an issue where possible rejection by the body is feasible. CNT offer mechanical advantages over the polymers or peptide fibers currently used in bone scaffolds. Zhao *et al.* (2005), investigated the use of chemically functionalised SWCNT as a scaffold material for the growth of artificial bone, they identified the potential for the self-assembly of HA on the surface of SWCNT. They suggested that this was possibly due to the presence of negatively charged functional groups on the SWCNT that attract the calcium cations present in HA (Zhao *et al.* 2005). The group also proposed that it is the high tensile strength, high degree of flexibility, and low density of CNT that make these materials ideal for the production of bone. The diameters of SWCNT used in the study by Zhao *et al.* (2005) are of similar order and magnitude to the triple helix collagen fibres within bone, and as such can act as scaffolds for the nucleation and growth of HA.

The potential for CNT to be used within bioengineering applications is by no means endless, however while many more applications could be discussed, the following papers offer further information on the use of nanotechnology for biomedical applications: Sinha and

Yeow (2005), Webster *et al.* (2004) and Bellare *et al.* (2002). Investigations concerning the cytotoxic response of CNT-containing materials have reported encouraging results confirming their potential use in orthopaedic applications (Smart *et al.* 2006); however, many questions remain unanswered and as yet, the understanding of the toxicity and biocompatibility of CNT-reinforced materials is not fully established.

12. CNT-reinforced bone cement

12.1 Mechanical properties

MWCNT offer the potential to augment mechanical properties of PMMA bone cement due to their strength and aspect ratio. The addition of MWCNT to PMMA bone cement has been shown to significantly improve the static mechanical properties (Marrs *et al.*, 2006 and Marrs, 2007; Ormsby *et al.*, 2010a; Ormsby *et al.*, 2010b), and the fatigue performance of MMA-co-Sty copolymer based bone cement (Marrs *et al.*, 2006). Marrs *et al.* (2006) investigated the influence of unfunctionalised MWCNT in PMMA based bone cements. They reported moderate improvements (13-24 %) in the static properties when 2 wt. % MWCNT was incorporated into PMMA bone cement. Marrs (2007) reported significant improvements (>300 %) in the dynamic properties of methyl methacrylate-styrene copolymer (MMA-co-Sty), a chief component of commercial bone cement when unfunctionalised MWCNT (2 wt. %) were added. However, both studies (Marrs *et al.*, 2006 and Marrs, 2007) used non-clinically relevant methods to ensure optimal dispersion of the MWCNT. The MWCNT were dispersed through a molten matrix of pre-polymerised commercial bone cement powder using stainless steel counter rotating rotors in a mixing chamber at 220 °C. The two materials were heated and subjected to high-shear mixing. Once the molten composite had cooled and hardened, it was crushed into pellets and hot pressed under vacuum to form films. These films were subsequently machined into testing specimen. Each specimen was then annealed at 125°C for a minimum of 15 h to alleviate any residual stresses that formed during machining.

The uniform distribution of CNT within the polymer matrix is critical for maximising the interfacial bond between the CNT and polymer matrix and therefore achieving optimal improvements in mechanical properties (Andrews *et al.*, 2002; Marrs, 2007). It has also been reported that alignment and optimum dispersion of the CNT is important in the context of improving the thermal properties of a nanocomposite (Xie *et al.*, 2005). The CNT must create a well dispersed, overlapping network facilitating the transport of electrons, phonons, and heat energy.

Many processing techniques have been employed to uniformly disperse CNT within polymer matrices (Xie *et al.*, 2005; Andrews *et al.*, 2002). The two most commonly used techniques involve (i) *in situ* dispersion (sonication of the CNT in solution) and (ii) high temperature shear mixing. These techniques are primarily used to separate the entanglements and agglomerations of the as-produced CNT, and secondly to disperse the individual CNT throughout the matrix. Andrews *et al.* (2004) stated that these techniques produce more favourable results when small concentrations of CNT are used, however, mixing higher concentrations of CNT (>5 wt. %) increases the viscosity of the mixture irrespective of the state of the polymer. Andrews *et al.* (2002) postulated that an elevated viscosity hinders effective dispersion of the CNT into the polymer matrix, therefore, the energy induced into the mixing process must be increased, but, at the risk of shortening the CNT or irreversibly damaging the matrix material. Moreover, it has been reported that the

efficacy of MWCNT reinforcement is largely dependent on the level of loading of MWCNT, the dispersion of these MWCNT and the peak stress of dynamic loading cycle (Marrs *et al.*, 2006; Marrs, 2007).

Ormsby *et al.* (2010a) addressed the limitations of the studies by Marrs *et al.*, (2006; Marrs, 2007) by incorporating unfunctionalised (MWCNT-UNF) and carboxyl (MWCNT-COOH) functionalised MWCNT (0.1 wt. %) into PMMA bone cement using three different preparation techniques. CNT were either added to the liquid MMA component of the cement via magnetic stirring or ultrasonic disintegration, or dry blended with the polymer powder component. A contemporary vacuum mixing system was subsequently used to mix the bone cement following the normal protocol for a joint replacement surgical procedure. Improvements in static mechanical properties and thermal properties of the MWCNT-PMMA nanocomposite cement were observed (Ormsby *et al.*, 2010a). Ormsby *et al.*, (2010a) demonstrated that adding MWCNT (0.1 wt. %) to the polymer powder or liquid monomer components prior to cement mixing with a proprietary mixing system, improved the mechanical properties of the resultant cement, provided the appropriate method for incorporating the MWCNT was used ($\approx 21\%$). This was a significant finding because mechanical failure of the bone cement mantle remains a major problem in joint replacement surgery (Topoleski *et al.*, 1990). Like typical fibre-reinforced composites, mechanical failure of PMMA bone cement is believed to take place in three phases, (1) crack initiation due to an initial imperfection in material stability, (2) slow crack growth, and (3) rapid propagation to fracture (Figure 25a) (Topoleski *et al.*, 1995). Although mixing the cement under the application of a vacuum and injecting the cement into the surgical site using a closed delivery system have improved the mechanical performance of the cement, residual material voids and poor surgical technique can contribute to weak or thin regions within the cement mantle causing these regions to be more susceptible to mechanical failure (Marrs *et al.*, 2006).

Ormsby *et al.*, (2010a) reported that adding MWCNT to the liquid monomer by magnetic stirring had an overall negative effect on the mechanical performance of the bone cement. This was largely attributed to the poor dispersion of MWCNT in the liquid monomer and resulting in MWCNT agglomerations within the cement matrix (Figure 25b).

These agglomerations acted as stress concentrations within the cement, providing a mechanism for premature failure of the cement when subjected to load. In contrast, dry blending MWCNT in the polymer powder or disintegrating the MWCNT in the liquid monomer using ultrasonic agitation suitably disentangled the nanotubes and homogeneously dispersed the MWCNT in the resulting nanocomposite (Ormsby *et al.*, 2010a). Andrews and Weisenberger (2004) also reported that ultrasonic disintegration was an effective method for dispersion of MWCNT at low levels (<5 wt. %) of concentration (Andrews and Weisenberger, 2004). Marrs *et al.* (2006) stated that care is needed when dispersing MWCNT within a polymer matrix, and reported the adverse effects of sporadic, inadequately dispersed, clumps of MWCNT, particularly at levels of loading greater than 5 wt. %.

The presence of well-dispersed MWCNT in PMMA cement with their anticipated strong nanotube-matrix bonding and high tensile properties, suggests that a percentage of the MWCNT would be orientated with their longitudinal axis perpendicular to the crack wave. Such MWCNT were effective in bridging the initial crack and preventing crack propagation, further enhancing the longevity of the cement mantle (Figures 25c and 25d), by improvement in mechanical properties. These improvements are clinically beneficial for the use of reinforced PMMA bone cement in TJR due to a reduction in the rate of crack

propagation. This effect may be most important for improperly placed femoral implants with thinner cement mantle layers, which continues to be cited as a factor that may reduce implant longevity (Morscher and Wirz, 2002). Additionally PMMA dental prostheses (dentures) are also known to fail prematurely through thin connectors due to impact and fatigue loading (Ormsby *et al.*, 2010a). There could be an application for MWCNT inclusion in PMMA dental prostheses, enhancing the functionality of denture-based acrylic materials when subjected to fatigue loading (Polyzois *et al.*, 1996).

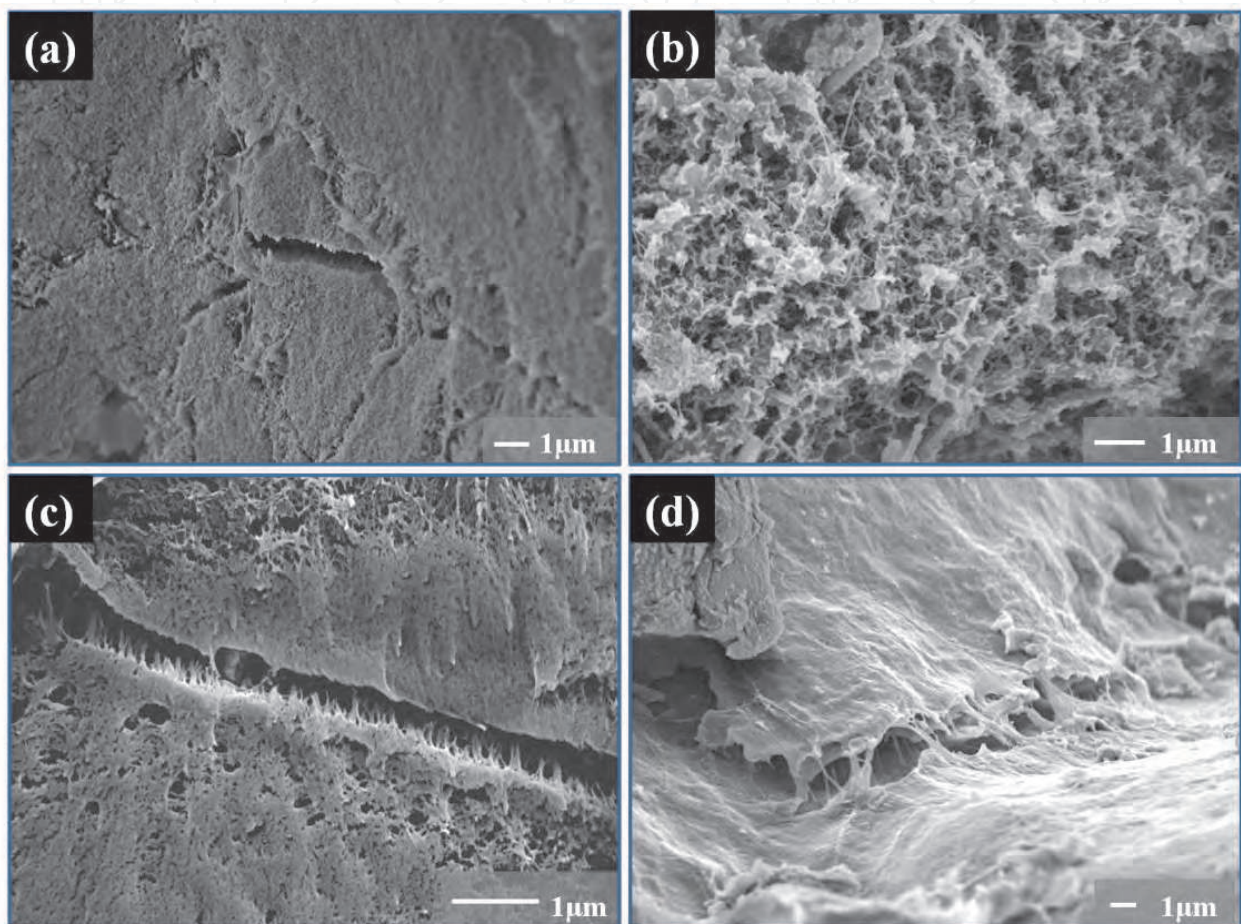


Fig. 25. SEM images showing (a) A large pore on the short rod chevron notched fracture surface of the control cement (X 300). (b) Unfunctionalised MWCNT dry blended in the PMMA polymer powder cement showing an agglomeration of barium sulphate, which was the fracture initiation point for this specimen (X 150). (c) Functionalised MWCNT disintegrated in the MMA liquid monomer by ultrasonication, MWCNT can be seen to bridge a micro-crack across the cement surface, X 5,000, (d) Functionalised MWCNT ultrasonically disintegrated within the MMA liquid monomer, MWCNT can be seen to bridge a micro-crack on the cement surface, X15,000 (Ormsby *et al.*, 2010a).

The filler/matrix interface in fibre-reinforced polymer composites is critical in controlling load transfer from the matrix to the fibre, failure mechanisms, and degradation (Ormsby *et al.*, 2010a). Gojny *et al.* (2003) reported that functionalisation of MWCNT led to reduced agglomeration and improved interaction between the nanotubes and the polymer resin. Ormsby *et al.*, (2010a) used MWCNT that were surface modified with a carboxyl grouping,

as it has been reported that the static mechanical properties of PMMA polymer resin can be significantly improved with this arrangement (Pande *et al.*, 2008). Ormsby *et al.* (2010a) observed that surface modification of the MWCNT with carboxyl groups did not result in significant improvements in the compressive or bend properties of the PMMA cement on a consistent basis. However, the fracture toughness of the PMMA cement was significantly enhanced (p -values <0.001) when the MWCNT were surface modified with carboxyl groups. It is unclear currently as to whether the improvements in performance of the MWCNT-PMMA cements are a direct consequence of good MWCNT dispersion within the PMMA matrix, providing mechanical reinforcement, or is due to a chemical interaction between the MWCNT and PMMA matrix (Ormsby *et al.*, 2010a). Eitan *et al.*, (2006) used strain dependent Raman spectroscopy to show that there is load transfer from the matrix to the nanotubes, and that the efficiency of the load transfer is improved by surface modification of the MWCNT.

It is also interesting to observe that significant improvements in fracture toughness did not correlate to improvements of the same magnitude for strength and modulus of the different cement combinations tested. Ormsby *et al.* (2010a) postulated that the methods adopted for specimen preparation, specimen configuration and the different modes of loading employed during testing could account for this. It has been reported that different loading regimes evaluate differing reinforcement mechanisms within the specimen microstructure, therefore dissimilar responses are expected (Lewis and Mladi, 2000; Wagner and Chu, 2006). Wagner and Chu (2006) also found distinctions in mechanical properties when testing three dental core ceramic based materials. They found significant differences in the biaxial flexural strength, but reported no significant difference for the indentation fracture toughness for the materials tested (Wagner and Chu, 2006).

Subsequent to this investigation, Ormsby *et al.* (2010b) also published a study investigating the efficacy of adding different concentrations of MWCNT to PMMA bone cement of varying functionality as a means of improving MWCNT dispersion and thus augmenting the mechanical properties of the PMMA bone cement further. The bone cement was prepared using the optimal method for MWCNT incorporation, as determined in their previous study (Ormsby *et al.*, 2010a). Ormsby *et al.* (2010b) reported that adding MWCNT at low loadings (≤ 0.25 wt. %) to MMA monomer, prior to cement mixing with a proprietary mixing system, improved the mechanical properties of the resultant nanocomposite cement. Adding carboxyl and amine functional groups enhanced the dispersion of the MWCNT within the cement matrix and potentially increased the interaction between the carbon nanotubes and the cement, thereby improving the mechanical integrity of the resultant nanocomposite cement. These improvements in mechanical strength are potentially significant as mechanical failure of the bone cement mantle remains a prevalent issue in total joint replacement surgery often leading to revision surgical procedures. Adding MWCNT at higher loadings (≥ 0.5 wt. %) provided a negative effect on the mechanical performance of the nanocomposite cement. This was attributed to poor dispersion of MWCNT resulting in agglomerations forming within the cement matrix. In contrast, low loadings (≤ 0.25 wt. %) of MWCNT were more readily disentangled by the application of ultrasonic energy and homogeneously dispersed in the resulting nanocomposite. The presence of well-dispersed MWCNT in PMMA cement with their anticipated strong nanotube-matrix bonding and high tensile properties, suggests that a percentage of the MWCNT would be orientated with their longitudinal axis perpendicular to the crack wave. Such MWCNT were effective in bridging the initial crack and preventing crack propagation,

further enhancing the mechanical integrity of the cement mantle. These improvements could have clinical benefits for the application of MWCNT-PMMA nanocomposite cement in TJR surgery, due to a reduction in the rate of crack propagation through the reinforced nanocomposite cement mantle. This effect may have greatest significance for misaligned femoral implants resulting in areas of thinner cement mantle thickness, which continues to be cited as a main factor of cement mantle failure (Ormsby *et al.*, 2010b).

Gojny *et al.*, (2003) also reported that the addition of chemical functional groups to the MWCNT can provide a negative charge to the MWCNT and thus reduced agglomeration and improve interaction between the nanotubes and the host polymer. The results of this study by Ormsby *et al.*, (2010b) concurred with the findings of Gojny *et al.* (2003). The PMMA bone cement with MWCNT-UNF exhibited least significant improvements (p -value <0.1) for all mechanical properties measured. This reduced improvement in mechanical properties was attributed to poor dispersion of MWCNT within the cement matrix, resulting in the occurrence of MWCNT agglomerations. The MWCNT-UNF provided a degree of mechanical reinforcement at lower loading (≤ 0.25 wt. %), largely due to the reduced tendency for MWCNT agglomerations. MWCNT-COOH provided the most significant (p -value <0.001) improvements in all mechanical properties of the PMMA cement. It is proposed these significant improvements are a result of a homogenous dispersion of the MWCNT within the PMMA matrix aided by the negatively charged carboxyl groups. This homogeneous dispersion in tandem with interfacial interactions between the functionalised MWCNT and PMMA matrix could provide improved mechanical properties of the resultant nanocomposite. The bone cements incorporating amine functionalised MWCNT (MWCNT-NH₂) also improved mechanical properties. These improvements were less significant p -value <0.01 when compared with the addition of MWCNT-COOH. It is postulated that this is due to the lower level of functional groups present on the MWCNT-NH₂ when compared with the MWCNT-COOH (that is 0.5% vs. 4.0%, functional groups, respectively). This lower concentration of MWCNT-NH₂ functional groups may result in a more heterogeneous dispersion of the MWCNT within the cement matrix, therefore resulting in a less successful transfer of stress through the cement mantle.

12.2 Thermal properties

PMMA bone cement is produced by a free radical reaction on mixing the polymer powder and liquid monomer constituents. The polymerisation reaction is a highly exothermic chemical reaction and as a consequence the peak temperatures typically reach 80-100 °C. It has been reported that polymerizing bone cement has the potential to cause thermal necrosis of the surrounding bone cells, which is one of the mitigating factors for aseptic loosening of an implant fixed with PMMA bone cement (Dunne and Orr, 2002).

Reducing the polymerisation reaction of PMMA bone cement, therefore lowering the extent of thermal necrosis has been investigated by many research groups. Meyer *et al.* (1973) reported reducing the temperature (22 °C) prior to bone cement mixing had a significant influence on the polymerisation reaction of the PMMA cement. They concluded that mixing PMMA cement at a temperature of 4°C resulted in a peak temperature (T_{\max}) of 53 °C, while mixing the same cement at 37 °C increased the peak temperature to 125 °C. Meyer *et al.* (1973) also investigated the effects of pre-chilling the femoral prosthesis prior to implantation into the bone cavity; they found adopting this approach did not influence the peak temperature. Larsen *et al.* (1991) also investigated the effects of pre-chilling the femoral prosthesis, however, they reported a 5 °C reduction in the peak temperature at the bone-

cement interface. Additionally, Lidgren *et al.* (1987) found using chilled water to pulse-lavage the bone cavity prior to cement delivery had a significant effect on the extent of the polymerisation reaction, the peak temperature was subsequently reduced from 59 °C to 45 °C. The mixing method used to prepare the PMMA bone cement prior to delivery into the bone cavity also has a role in its polymerisation reaction. Dunne and Orr (2002) reported the level of heat generated for bone cement prepared under the application of a vacuum was significantly reduced when compared to the same cement prepared under atmospheric conditions using a bowl and spatula mixing arrangement. Other methods can be used to reduce the degree of polymerisation reaction of PMMA bone cement, such as altering the compositions or constituents of the cement. However, this can have a significant influence on the mechanical and handling performance of the bone cement (Lewis *et al.*, 2007).

CNT incorporation has previously been reported to improve the thermal properties of a range of polymers, including polyethylene (McClory *et al.*, 2010), polyurethane (Marrs *et al.*, 2006), polystyrene (Andrews and Weisenberger, 2004), polyvinyl alcohol and methyl methacrylate-styrene copolymer (Xie *et al.*, 2005).

Andrews and Weisenberger (2004) proposed that the thermal property improvements for CNT-polymer composites are a function of CNT type, degree of dispersion, CNT loading, CNT alignment and polymer matrix. Xie *et al.* (2005) reported a significant improvement ($\approx 125\%$) in the thermal conductivity of an epoxy when 1.0 wt. % SWCNT powder was added. Choi *et al.* (2003) observed an increase ($\approx 300\%$) in the thermal conductivity of an epoxy for a SWCNT loading of 3.0 wt. %. The thermal properties of PMMA bone cement have been modified with MWCNT by Ormsby *et al.*, (2010a). Incorporating either unfunctionalised or carboxyl functionalised MWCNT into the PMMA powder or liquid monomer prior to mixing both components together had a significant effect on the exothermic polymerisation reaction. It was observed that maximum temperature and the setting properties exhibited during polymerisation were significantly reduced by the inclusion of 0.1wt. % (unfunctionalised or carboxyl functionalised) MWCNT into the PMMA cement, irrespective of the method of introduction. Other studies have also reported reductions in the thermal properties of PMMA cement on addition of 5-15 wt. % steel fibres (Kotha *et al.*, 2002). Dunne and Orr (2002) reported that reduction of the polymerisation exotherm will decrease the likelihood of residual stresses developing within the cement mantle, which can cause premature failure of the cement when subjected to mechanical loading.

The importance of minimising the bone cement exothermic reaction has been stressed, as it may result in a permanent cessation of blood flow and bone tissue necrosis, which shows no sign of repair after 100 days (Moritz and Henriques, 1947; Feith, 1975; Eriksson and Alberksson, 1983; Mjoberg *et al.*, 1984). The cumulative TNI (Thermal Necrosis Index) has been used previously to assess the level of irreparable damage bone cement caused by heat generation (Moritz and Henriques, 1947; Dunne and Orr, 2002). If TNI exceeds one there is the possibility of thermal damage to the living tissue cells. The thermal necrosis index is typically calculated at two temperatures; >44 °C and >55 °C, chosen because the temperature threshold for impaired bone regeneration has been reported to be in the range of 44-47 °C (Moritz and Henriques, 1947; Eriksson and Alberksson, 1983). The incorporation of MWCNT to PMMA based bone cement may reduce the incidence of polymerisation induced hot spots and thermal necrosis of the surrounding tissue adjacent to the cement mantle, which is believed to be observed radiographically (Linder, 1977). Reducing the occurrence of such tissue damage may improve the mechanical integrity of the cement-bone interface, thereby promoting implant longevity.

Ormsby *et al.*, (2010a) report that the incorporation of unfunctionalised or carboxyl functionalised MWCNT assisted in the dissipation of the heat produced during the exothermic polymerisation reaction of PMMA bone cement, irrespective of the method of introduction. With unfunctionalised MWCNT, this reduction was not below the levels necessary to prevent thermal tissue damage as the TNI was greater than one. In contrast, surface modification of the MWCNT with carboxyl groups and subsequent addition to the liquid monomer using magnetic stirring did reduce the TNI values at >44 °C and >55 °C to levels below one.

In a subsequent study by Ormsby *et al.*, (2011) the incorporation of unfunctionalised, amine, and carboxyl functionalised MWCNT at increasing wt. % assisted in the dissipation of the heat produced during the polymerisation of PMMA bone cement. It was observed that any effect on the reaction exotherm was dependant on MWCNT loading. The greater reductions in exotherm were reported for the highest level of MWCNT loading (1.0 wt. %). Saha and Pal (1986) reported a similar finding when examining carbon fibre reinforced bone cement. The greatest reductions in peak exothermic temperature were associated with the highest levels of carbon fibre. It is important to note that the types of MWCNT used within the study by Ormsby *et al.*, (2011) had thermal conductivity values of $>3000\text{Wm}^{-1}\text{K}^{-1}$. It was therefore proposed that the MWCNT act as a heat sink within the PMMA bone cement and therefore assist in the dissipation of the heat generated during the polymerisation reaction (Ormsby *et al.*, 2011). This behaviour is also a function of the extent of MWCNT dispersion and distribution throughout the PMMA bone cement matrix, such that uniform dispersion of MWCNT within the cement will dissipate the thermal energy throughout the cement matrix. This is further aided by the interconnectivity of MWCNT entanglements and the very large surface area of MWCNT ($600\text{-}1000\text{ m}^2/\text{g}$) (Peigney *et al.*, 2009). Bonnet *et al.* (2007) found a similar effect on the addition of 7 vol. % of SWCNT to PMMA reporting a 55 % increase in the thermal conductivity. It is therefore hypothesised that the thermal conductivity of the PMMA bone cement described here will have also increased due to MWCNT addition.

It has been stated that for composites incorporating CNT to be thermally conductive, they must form a percolated network of overlapping or touching CNT for the transport of heat energy (Marrs, 2007). Therefore bone cements with relatively poor levels of MWCNT dispersion (≥ 0.5 wt. %) within the PMMA matrix, due to agglomerations (Figure 26), demonstrated the greatest reduction in thermal properties.

It is possible to use this theory to explain why the MWCNT of different chemical functionality provided differing thermal properties. The addition of MWCNT-UNF and MWCNT-NH₂ provided more significant reductions in the polymerisation reaction when compared to the MWCNT-COOH. It is suggested by Ormsby *et al.*, (2011) that this may be due to a less homogeneous dispersion of the MWCNT-UNF and MWCNT-NH₂ within the cement in comparison to the improved dispersion of the MWCNT-COOH.

Ormsby *et al.* (2010b) added MWCNT of various chemical functionality at increasing loadings to PMMA cement and assessed the mechanical properties of the resultant composites. They reported significant improvements in mechanical properties at low levels of MWCNT loading (≤ 0.5 wt. %). Ormsby *et al.* (2010b) showed that MWCNT-COOH provided the greatest improvement in mechanical properties, due to the improved MWCNT dispersion associated with improved interfacial interactions between these MWCNT and PMMA through enhanced van der Waals attraction and hydrogen bonding.

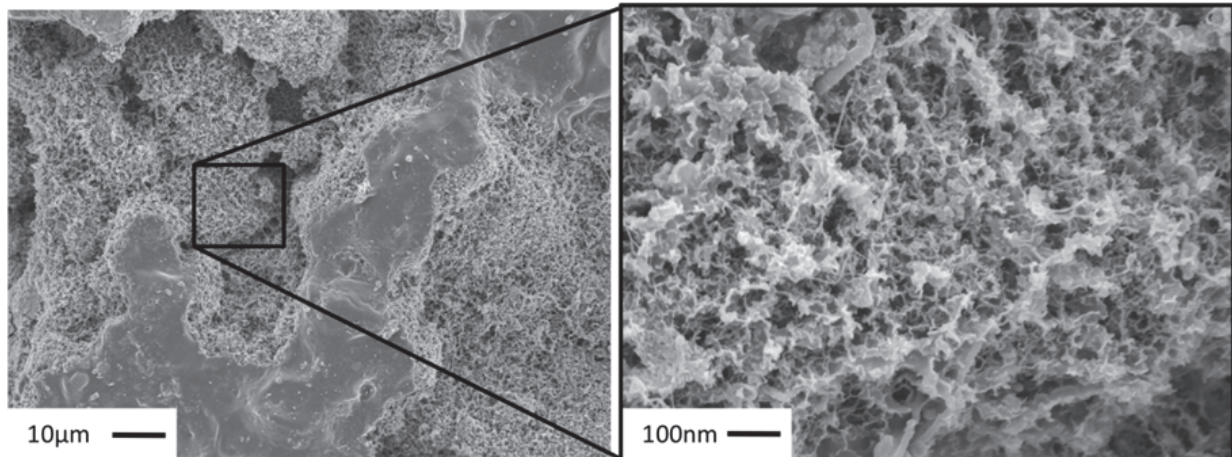


Fig. 26. SEM image of 1.0 wt% MWCNT filled PMMA bone cement showing MWCNT-UNF.

It is noteworthy that the MWCNT inclusion altered the rate of PMMA polymerisation. A slower rate of polymerisation extended the time taken for the bone cement to fully polymerise, which in turn reduced the T_{max} and TNI values. It is postulated that the presence of MWCNT in the cement not only altered the kinetics of the polymerisation reaction, but additionally played a role dissipating heat energy. Incorporation of carboxyl and amine functionalised MWCNT had a greater influence on the polymerisation reaction of the bone cement used in this study, compared to the unfunctionalised (Ormsby *et al.*, 2011).

12.3 Rheology properties

The efficacy of PMMA bone cement in anchoring a TJR is affected by many fundamental characteristics. Among these are the rheological, polymerisation, and handling properties, whose significance is two-fold (Ormsby *et al.*, 2011). Firstly, the ease with which the cement flows into the intramedullary bone canal facilitates the controlled positioning of the prosthesis. This is critical as it has been reported that initial prosthesis position is a contributory factor to the longevity of the cemented implant (Jones *et al.*, 1992; Lewis and Carroll, 2001). Secondly, the rheological properties of the cement may play an important role in the development of pores in the cement during mixing and delivery. Such pores may act as sites for the initiation of cracks, which, in turn, can cause or contribute to aseptic loosening of the prosthesis (Jones *et al.*, 1992).

To date, there have been limited studies examining the viscoelastic properties of PMMA bone cement, with oscillatory shear rheometry (OSR) being the most common method employed. Harper *et al.* (2000) observed that the complex viscosity (η^*) of VersaBond™ and Palacos® R cements increased from 1000 Pa.s at 2.5 min to 5000 Pa.s at 6 min. They defined this sharp increase in η^* as the onset of cure. Spiegelberg and McKinley (1998) determined the critical gel time of Simplex P™ cement as 9.7 min. Farrar and Rose (2001) investigated the initial polymerisation reaction of several commercial bone cements. They examined η^* over a range of temperatures and concluded the polymerisation of bone cement is strongly dependent on temperature. Ormsby *et al.*, (2011) have assessed the influence of differing MWCNT (unfunctionalised, carboxyl functionalized or amine functionalised) on the rheological properties and cure kinetics of the polymerising PMMA bone cement. They investigated how the differing MWCNT systems influenced the time at which the onset of polymerisation occurred, as well as the time at which polymer gelation occurred. Ormsby *et al.*, (2011) found that MWCNT addition significantly influenced the rheological behaviour of the polymerising

cement. For each cement investigated, η^* increased with time. Ormsby *et al.*, (2011) explained this trend applying the Krieger–Dougherty equation (Equation 1) (Krieger and Dougherty, 1959), which describes the viscosity of a concentrated suspension (η).

$$\eta^* = \eta_s \left(1 - \frac{\varphi}{\varphi_m} \right)^{-[\eta] \varphi_m} \quad (1)$$

where, η_s is the viscosity of the suspending medium, φ is the phase volume of the particles in the suspension, φ_m is the maximum packing fraction of those particles, and η is the intrinsic viscosity. This equation may be used to comment on the variation of the polymerizing bone cement's η^* as a function of time, although its application is limited as it primarily applies to Newtonian suspensions. During the initial stages of mixing the powder and liquid components, the high initial viscosity is attributed primarily to the swelling of the polymer beads within the cement powder (Lewis and Carroll, 2001). As elapsed time from start of mixing increases and swelling causes both φ_m and η to decrease. Thus, η^* increases with t , a trend observed in the present results of the studies of Lewis and Carroll, (2001), and Ormsby *et al.*, (2011).

Ormsby *et al.*, (2011) found that the incorporation of chemically functionalised MWCNT (MWCNT-COOH and MWCNT-NH₂) into PMMA bone cement significantly extended the onset of cure. This effect was more pronounced as MWCNT loading was increased. Indicating the time delay before the onset of cure for these composite cements is in part due to the role the functional groups play in altering the polymerisation reaction, in addition to physically preventing cross-linking of the polymer chain. The onset of cure of the PMMA cements with MWCNT-UNF addition was also delayed, but to a lesser extent. In all cases, MWCNT addition to PMMA bone cement prevented macro-gelation from occurring.

It was also significant to observe that on addition of MWCNT-COOH, gel-times increased up to a loading of ≤ 0.5 wt. %, but at 1.0 wt. % the gel-time decreased, compared to the control sample. This finding is commonly reported for heavily-filled polymers, as the cement may exhibit solid-like properties from the onset of mixing. Therefore, initially the filled bone cement will have a higher viscosity than the control, but the actual onset of polymerisation may not occur until much later in the reaction. Lalko *et al.* (2009) reported a similar behavior after incorporating increasing fractions of functionalised CNT into polycarbonate.

Lower loadings of MWCNT-COOH (≤ 0.5 wt. %) did extend gel-times, when compared to the control (MWCNT free bone cement), again supporting the hypothesis that the reduced rate of polymerisation is due to chemical interactions between functional groups present on the surface of the MWCNT and the polymer matrix, as the time before gelation occurs increased with level of loading (and thus concentration of functional groups). Ormsby *et al.*, (2011) have suggested that the physical presence may indeed affect the rate of polymerisation, but the functional chemical groups may be the predominant influence.

This hypothesis is supported by the theory that if the functional groups on the MWCNT were indeed interrupting the polymerisation reaction by terminating polymer chains via formation of covalent bonds, then the onset of cure (sudden increase in complex viscosity) would never occur and the cement would never reach a hardened state. It is noteworthy though, for this to occur, the MWCNT loading would need to be significantly higher than 1.0 wt. % (Ormsby *et al.*, 2011). Interestingly, the gel-times remain relatively unchanged for

the bone cement with MWCNT-UNF, with no clear pattern evident irrespective of MWCNT-UNF loading. These results would indicate that the prolonged time before the onset of cure experienced in the bone cements with MWCNT-COOH is dependent on the carboxyl functional group.

13. Summary and conclusions

As the number of primary TJR continues to increase each year and, even with the reported decrease in the proportion of cemented TJR performed, PMMA bone cement is still required for the majority of TJR procedures. At present with longer life expectancy and younger patient populations requiring TJR, an increase in cemented revisions seems inevitable. Aseptic loosening is continually cited as being the most common indication for revision. It is well established that for cemented implants a number of factors contribute to aseptic loosening, of which, fatigue damage of the cement mantle has been observed *in vivo*. Therefore, a crucial requirement exists for the development of new technologies and biomaterials for the treatment of traumatic injuries and chronic diseases, which allow less tissue damage and more tissue regeneration and are conducive to rapid patient recovery. Particularly for biomaterials and devices designed to replace a degenerated or diseased joint, bone structure, many questions need to be answered. Such devices and implants would benefit significantly from availability of a material that is multi-functional and can meet the biomechanical and biological requirements.

The conventional biomaterials available today are reaching their maximum capabilities, notwithstanding their successful application in treating and preventing different medical conditions. There is a need for the development of new biomaterials which must satisfy several requirements ranging from physical, mechanical, biological, toxicological and other characteristics, depending on the final clinical application.

Carbon is chemically inert and CNT not only demonstrate superior mechanical, chemical and electrical properties, but also have the potential to be biocompatible particularly when appropriately functionalised. Also, encapsulation of other materials within CNT could potentially create applications for therapeutic use in medicine. Incorporation of MWCNT into PMMA based orthopaedic bone is a case in point, whereby a high degree of MWCNT-polymer matrix interaction has been shown to increase the fracture resistance during mechanical loading. Furthermore, it has been reported that MWCNT-PMMA bone cement leads to increased viscosity and reduced polymerisation temperatures. Reducing the temperature generated during polymerisation could reduce the thermal cellular necrosis experienced *in vivo*, reducing the probability of aseptic loosening. Furthermore, a reduction in the exotherm of bone cement will reduce residual stresses within the cement mantle as a consequence of excessive shrinkage.

To fully exploit the use of MWCNT in PMMA bone cement further development and research is required. In particular a detailed investigation of the biocompatibility of the MWCNT composite cements is required. This would require exposing human osteoblast cells to the composite MWCNT-PMMA bone cements, ultimately leading to *in vivo* cell work. This would provide a clearer indication of the MWCNT composite cements potential integration into the body.

Regardless of this interest, there are many issues and limitations to be considered. The field of nanomaterials for biomedical and bioengineering applications is still very much in its infancy and many difficult questions remain unanswered, including manufacturing, safety

and regulatory issues. Preliminary investigations substantiate the enormous potential of MWCNT systems for biomedical and bioengineering applications either as a structure, coating, scaffold or composite; although most of these are only at laboratory-scale and *in vitro* testing. There is a major requirement for interdisciplinary collaboration and exchange of knowledge at many levels to effectively address the current issues, before being able to fully understand and explore the true potential of CNT for biomedical and bioengineering applications.

14. References

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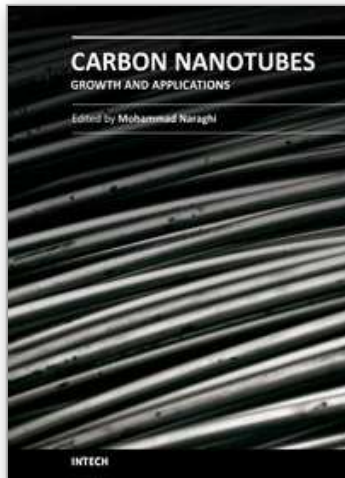
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Carbon Nanotubes are among the strongest, toughest, and most stiff materials found on earth. Moreover, they have remarkable electrical and thermal properties, which make them suitable for many applications including nanocomposites, electronics, and chemical detection devices. This book is the effort of many scientists and researchers all over the world to bring an anthology of recent developments in the field of nanotechnology and more specifically CNTs. In this book you will find:

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