Review

Carbon nanotube reinforced hydroxyapatite composite for orthopedic application: A review

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ABSTRACT

Application of hydroxyapatite (HA) in orthopedic implants suffers from its low fracture toughness and poor wear resistance. Carbon nanotube (CNT), with its high stiffness and mechanical strength, is an attractive reinforcement for HA to surmount these issues. The last 7–8 years have seen a number of studies to explore the efficiency of CNT reinforcement in strengthening HA, in the form of composites and coatings. Impressive improvement in the fracture toughness and wear resistance of HA with CNT reinforcement and beneficial effects on biocompatibility has sparked further research interests, for possible clinical applications. This review article aims to cover a wide span of this exciting and expanding research arena – from detailed technical discussions on HA–CNT system, their processing techniques and the influence of CNT dispersion in the HA matrix. Role of CNT in the improvement of mechanical properties and tribological behavior of the composite has been discussed in light of different processing techniques. Other important issues related to HA–CNT system, e.g., phase transformation and crystallinity of HA and HA–CNT interfacial bonding has been stressed upon. Biocompatibility of HA–CNT composites, which is extremely important for its intended orthopedic application, has been summarized with an overview of the present status. An in-depth analysis of the information presented in this review facilitates a better understanding of the current state of HA–CNT research and allows framing guidelines toward future research direction for its successful clinical application.

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Keywords:
Carbon nanotubes
Hydroxyapatite
Orthopedics
Biocompatibility
Wear
Fracture toughness

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1. Introduction

The field of biomaterials is a rapidly emerging one, due to its direct relation with the healthcare and impact on human health related issues. The biomaterials device market was $115.4 billion in the year 2008 and is expected to be $252.7 billion in 2014 [1]. The largest market size among all biomaterial products belongs to orthopedic biomaterials. As a result, development and improvement of orthopedic related biomaterials is a very active and growing research field.

Orthopedic biomaterials are mainly of two types. The first ones are implants and accessories, which are generally made of metals, ceramics, hard polymers or their composites. Second category consists of scaffolds for tissue regeneration, which are based on polymers - preferably the biodegradable ones and their composites. While discussing the orthopedic biomaterials, hydroxyapatite (HA) is very attractive for implants due to its chemical composition, which is similar to the apatite found in bone. The bioactivity and osteoconductivity of HA offer a suitable surface for new bone growth and integration [2–6]. Thus, HA is being vastly researched and used as freestanding implant parts, coating on metallic implants and also as reinforcement to polymer scaffold material for tissue regeneration [2,5–7,13].

But the main shortcomings of freestanding HA implant or HA coatings are their poor fracture toughness and wear resistance [3–5,14,15]. One of the most suitable solutions of this problem is reinforcement of a second phase material. Researchers have explored the possibility of using other hard ceramics [16–21], polymers [22,23] and bio-glasses [24] also. Keeping in concern the biocompatibility of the composite structure, the ideal reinforcement material is the one that can increase the fracture toughness and wear resistance significantly with a very low content of reinforced phase. Carbon nanotubes (CNT), with their excellent stiffness and strength, possess good potential for this purpose. CNT possesses Young’s modulus in the range of 200–1000 GPa [25] and tensile strength of 11–63 GPa [26]. Several studies on CNT reinforced metal/ceramic/polymer matrix composites have successfully demonstrated its capability of improving the structural properties, e.g., the strength, elastic modulus, fracture toughness, wear resistance etc. [27–29]. Further, the biocompatibility of CNTs in orthopedic application is also established by studies showing accelerated bone growth (in-vitro) [30] and increased proliferation and differentiation of osteoblast (in-vitro) [31–34] in the presence of CNTs. The recent report on biodegradation of CNT by human neutrophil and macrophage [35] strengthens the drive for bio-related applications of CNTs. Though, the biocompatibility of CNT is still not in a universal agreement due to contradictory reports, but the cytotoxic effect of CNT is mostly attributed to other factors, e.g., presence of metallic catalyst particles, agglomeration etc. and not due to CNT itself [36–38]. Moreover, CNTs are found promoting bone growth [30] and osteoblast proliferation [31–41], which fortifies its candidature as orthopedic biomaterial.

Consequently, CNT has emerged as a potential reinforcement for HA to solve its fracture toughness and wear resistance related problems. Research on HA–CNT composites has started very recently in 2004 [42,43]. The chronological trend of publications on HA–CNT system, as shown in Fig. 1, presents a clear visualization of the growing interest in this field. A significant increase in the number of publications in 2010 and 2011 indicates the growing importance of this topic in the contemporary research on this system.

![Fig. 1. Year-wise publication plot for HA–CNT system. Source: Scopus.com.](image-url)
research. With the significant amount of ongoing research work in this field – it is the right time to have a comprehensive review of the current state. Such a review will provide a complete picture of advancement in this field for understanding the current status of research and findings. It would also point out the areas requiring attention and will thus help in determining the direction of further research.

The importance of HA–CNT system was efficiently recognized by White, Best and Kinloch at an early stage of development in 2007, which insisted them to publish a brief review article in this topic [3]. Their review article dwells on the reasons behind using CNT as reinforcement to HA for orthopedic application with its probable advantages and challenges. But HA–CNT research in 2007 was still in its infancy with only 13 papers published, out of which 8 were summarized by White et al. in their review [3]. One of the major research focuses on HA–CNT system is on the composite coatings that have the potential to replace the clinically used HA coatings on metallic implants, with improved mechanical and tribological properties. There were only two studies on HA–CNT coatings (by laser surface alloying) published before 2007 [44,45]. Afterwards, different coating methods, namely, plasma spraying, electrophoretic deposition and aerosol deposition have been successfully applied to synthesize HA–CNT coatings on metallic surfaces. The information available on the improvement of mechanical properties of HA with CNT reinforcement was also scanty at the time of the previous review in 2007. Thorough studies on fracture toughness, stiffness, flexural strength, hardness and other mechanical properties as well as tribological behavior of HA–CNT composites have taken place afterwards, which need a detailed account and analysis to understand the trend. Moreover, no study on biocompatibility assessment for HA–CNT was available at the time of the previous review by White et al. [3]. At present, quite a few publications reported biocompatibility of HA–CNT composite systems using various assessment techniques, mostly in-vitro in nature. Thus, it is necessary to understand the biocompatibility of HA–CNT system in orthopedic implants.

In this present scenario, we present here a comprehensive review on the studies available on HA–CNT system. The review includes all issues regarding the processing of HA–CNT composite, effect of CNT addition on its mechanical and tribological behavior and its biocompatibility. The review provides a thorough and analytical insight to the overall development of HA–CNT composite system in a comparative mode with the underlying challenges that need to be addressed. All the studies on HA–CNT have used multiwall CNTs as reinforcement. Thus, multiwall CNT is referred as CNT in this study.

2. HA–CNT composite powder/precursor preparation

Homogeneous distribution of the second phase reinforcement plays a key role on the performance of HA–CNT, like all other composite systems. Dispersion becomes even more critical owing to the natural tendency of CNTs to form agglomerates due to their high aspect ratio and higher surface energy. Several modifications in the composite processing techniques have been adopted to ensure homogeneous dispersion of CNTs in HA at powder/precursor stage itself. Fig. 2 presents the classification of different powder/precursor processing techniques reported for HA–CNT system. The main aims of these methods are (i) to ensure better dispersion and avoid agglomeration of CNT in HA matrix; (ii) better interaction of CNT with HA at the interface to ensure good bonding in the composite. The following sub-sections briefly discuss each of the powder preparation techniques with a summary of their outcomes.

2.1. Chemical mixing methods

Chemical methods include chemical synthesis of HA on CNT surface and vice versa or chemical modification of CNT surface for homogeneous distribution of two phases in powder/precursor stage.

2.1.1. Chemical precipitation of HA on CNT

Chemical precipitation of HA on CNT surface is generally performed by dispersing CNTs in the chemical bath from which HA is precipitated. CNT, thus coated with HA, ensures uniform distribution of HA and CNT, as well as, has a potential to improve the adhesion between nanotube and matrix. Most of the studies have suspended CNT in calcium nitrate bath followed by stirring. Afterwards, diammonium hydrogen phosphate is added to the bath with vigorous agitation to form HA precipitate on the surface of suspended CNTs [42,46–55]. Some of the studies have replaced calcium nitrate with calcium chloride [56,57]. Optimization of the precipitation parameters and specially pH (>10) ensures precipitation of HA phase and avoids formation of CaHPO₄·2H₂O or Ca₃(PO₄)₁₂ phases [47,52,53]. Further study by Lu et al. shows that precipitated HA crystal size is a function of the temperature [52]. It is also mentioned that HA crystals prefer growing along the c-axis and bigger crystals are not good for the coating due to their small contact area [52].

Most of the studies report uniform distribution of CNTs in the HA precipitate in powder form using the chemical precipitation method. The only exception is reported by Keally et al. on formation of HA aggregation in the resulting precipitate, though, no major change in

![Fig. 2. Classification of techniques adopted for better dispersion of CNT in composite powder/precursor (for coatings).](image-url)
the precipitation parameters is noted [51]. HA precipitate formed on the CNT surface by chemical precipitation route is amorphous that requires hydrothermal treatment for crystallization [42,57]. Fig. 3 shows uniformly coated CNT with amorphous and crystalline HA precipitates, before and after hydrothermal treatment respectively, as observed by Zhao and Gao [42].

2.1.2. Functionalization of CNT

Functionalization of CNT is basically acid etching of its surface and attaching functional groups like $\text{COOH}$, $\text{OH}$ and $\text{C}=\text{O}$, resulting in a negatively charged nanotube surface. These anionic groups attract positively charged ions and particles to get attached on the CNT surface. The purpose of functionalization is twofold: (i) forming good bond between HA and CNT at powder/precursor stage and (ii) obtaining homogeneous dispersion of CNT by forming coating of HA on its surface. Functionalization of CNT is carried out by refluxing with the HNO$_3$–H$_2$SO$_4$ mixture [50,58–65] or HNO$_3$ only [52,56,57,66].

Functionalization of CNTs is found as an essential step before chemical precipitation of HA on CNT [50,52,55–57]. The negatively charged functional groups on CNT surface first get attached with the Ca$^{2+}$ ions through electrostatic attraction. Subsequently, PO$_4^{3–}$ ions are introduced in the bath, which react with Ca$^{2+}$ and forms HA precipitate. Functionalization of CNT is also found effective in preparing the precursor for coating synthesis using electrophoretic [58,59,62] and aerosol deposition [61]. The aqueous suspension of HA is adjusted (pH = 4) to get the HA particles positively charged for the uniform dispersion in the precursor. Functionalized CNTs, being introduced in the suspension, attract positively charged HA particles through electrostatic force to form coating on them [62]. TEM and SEM observations of the composite powder from such precursor have found CNTs mostly covered by fine HA particles, revealing effectiveness of functionalization [59,61,62].

2.1.3. Chemical vapor deposition of CNT on HA

Chemical vapor deposition (CVD) process is used to grow CNT on HA powder to ensure better dispersion and bonding of CNT with HA. Another advantage of using CVD grown CNT in composite is claimed to be retaining the undamaged pristine CNT structure while powder processing [67–69]. CVD technique has been applied successfully for different metal and ceramic matrix composites to get homogeneous dispersion of CNT in the matrix [70,71]. CVD route for preparing composite HA–CNT powders is proposed by two different groups [67–69,72,73]. Li et al. used Fe catalyst (0.4–10 wt.%) on HA powder to grow CNT and reported increasing CNT content in composite powder with increasing Fe content [67]. But, Lu et al. have directly used HA powders as catalyst to grow CNT, thus avoiding addition of metallic catalyst particles [68]. Though, they have observed decomposition of HA to some extent in the process of in-situ CNT growth. Catalyst particles (Fe and HA) were found encapsulated in the as-grown CNT in both the studies. Fig. 4 shows Fe catalyst particles encapsulated in CVD grown CNT on HA powder, as observed by Li et al. [67]. In another study, Li et al. have performed a comparative evaluation of the effect of Fe, Ni and Co catalyst particles on the quality of CVD grown CNTs on HA powder [69]. Their study revealed that highest growth rate and crystallinity of CNTs using Fe, whereas lowest growth rate and crystallinity were observed for Co. HA–CNT composite powder, prepared through CVD route, possesses homogeneous dispersion of CNTs and attribute toward strong bonding at reinforcement–matrix interface in the final composite structure [67].

2.2. Mechanical mixing methods

Mechanical methods of composite powder processing involve physical mixing of HA and CNT using mechanical forces. Often, mechanical mixing is augmented with chemical mixing to enhance CNT dispersion.

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**Fig. 3.** TEM images of CNTs–HA (a) before and (b) after hydrothermal treatment. Inset shows the EDS spectrum for HA layer in (a) [42].

**Fig. 4.** TEM image of Fe-catalyst particles encapsulated in CVD grown CNT on HA powder [67]. White arrows indicate Fe-catalyst particles retained in CNT.
2.2.1. Ball milling

Ball milling is used to disperse CNTs in HA to prepare composite powders for fabricating both coatings and sintered parts. Chen et al. have used ball-milling to mix up to 20 wt.% CNTs in HA for laser surface alloyed coatings [15,44,45]. Other research groups have used ball-milled HA–CNT composite powders for preparing composites using sintering [74], hot pressing [63,75] and spark plasma sintering routes [76]. Sarkar et al. have reported considerable dispersion of CNTs in HA powder with the presence of some agglomerates in the ball-milled composite powder [76]. But, these studies have not specifically mentioned about the effectiveness of ball-milling for dispersing CNT in HA [15,44,45,63,74–76].

2.2.2. Ultrasoundation

Ultrasoundation has been used both independently and in conjunction with chemical mixing methods to prepare HA–CNT composite powder/precursor. The very first study on HA–CNT mixing by ultrasoundation has reported this method to be more effective in dispersion than ball milling [74]. Ultrasoundation is mostly used in preparing HA–CNT composite precursor for ambient temperature coating techniques, e.g. electro-milling [74]. Freeze-drying of the composite powder, using liquid nitrogen after ultrasoundation led to homogeneous distribution of CNT in fine HA particles [64]. Wei et al. have used ultrasoundation as an aid for the improved dispersion of CNTs in chemically precipitated composite powder [46].

2.2.3. Mechanical agitation/stirring

Mechanical agitation methods, other than ball-milling and ultrasoundation, have also been used to prepare HA–CNT composite powder. Blending of HA powders with CNT in jar mill has been used for plasma sprayed coatings [14,83–85] and spark plasma sintered composite parts [86]. Mechanical stirring in ethanol up to 5 days has also been used for preparing composite HA–CNT powder as feedstock for spark plasma sintering [87–89]. Functionalization of CNTs and dispersion using surfactant in conjunction with mechanical mixing are also utilized for preparing composite powder [50,60,90]. A comparative study by White et al. has shown that functionalization of CNTs prior to mechanical mixing with HA improves the degree of dispersion [50]. The above mentioned mechanical mixing methods have reported good dispersion of CNTs in the HA matrix. But, use of agate mortar to make a slurry and then defoaming mixing by Tanaka et al. have resulted in an inefficient dispersion and formation of CNT agglomerate in the composite [91]. Similar observation is made by Keally et al. also, while using gyroscopic tumbler for HA–CNT mixing [51].

2.3. Other mixing methods

Some of the methods used for aiding the dispersion of CNT in HA at powder stage cannot be classified under purely chemical or mechanical mixing methods. Methods that use surfactant for dispersion of CNT and spray drying for preparing HA–CNT composite are described briefly in the following subsections.

2.3.1. Using surfactant for dispersion of CNT

Surfactants are mostly used in conjugation with other powder preparation techniques to prepare the composite powder. A thorough study by Meng et al. [90] on different surfactants for dispersing CNT shows that anionic surfactants, e.g., sodium dodecyl sulfate (SDS) or sodium dodecyl benzene sulphonate (SDBS) make better dispersion of CNTs in de-ionized water. Because the hydrophilic end of anionic surfactants is anionic and thus the cationic ends attach with negatively charged surface of the functionalized CNTs. Meng et al. have also observed that HA powders dispersed using cationic surfactants, e.g., cetyl trimethyl ammonium bromide (CTAB), get mixed more uniformly when dispersed in CNT bath with anionic surfactant. HA powder without surfactant does not lead to good dispersion of CNTs. The reason is natural attraction between the hydrophilic ends of cationic and anionic surfactants, helping in attachment of HA and CNT in the dispersion [90]. A recent study by Lei et al. has found polyvinyl pyrrolidone (PVP) to be a better surfactant than SDS [54]. PVP is found showing better wrapping, dispersion and ability to resist agglomeration of CNTs in water than SDS [54]. A few studies have used surfactant to disperse CNTs and then chemically precipitate or mechanically mix HA to prepare powder for composite [54,63,76,82] or precursor for coating [77].

2.3.2. Spray drying

Spray dried powders have been used for HA–CNT composite preparation mostly by our research group [14,32,83,85,92]. Spray drying is a process of preparing micron sized agglomerates of nano-sized powder by atomization. We have prepared spray dried composite HA–CNT powders by dispersing HA nano-powder and CNTs in water soluble organic binder, spraying in atomized chamber and then drying to get micron size spherical agglomerates [32,92]. Spray drying process is found effective in dispersing CNT in HA. SEM image in Fig. 6 shows the surface of a spray dried agglomerate showing individual CNTs dispersed in HA.

Fig. 5. SEM images of ultrasonically mixed HA–CNTs powder at (a) low and (b) high magnifications [79].
nano-particles [92]. Spray dried HA–CNT composite powders have also been used by our research group to synthesize composites via spark plasma sintering [92] and plasma spraying [32]. Balani et al. have used spray dried HA powder for plasma sprayed coatings, but CNTs were separately added to spray dried HA [14,17]. Few other studies have used spray dried HA powder and spray dried composite alumina–CNT powder to mix together mechanically [84–86]. The homogeneous dispersion of CNTs in alumina is reported to result in good dispersion of CNT in the final HA–alumina–CNT composite powder. A review of HA–CNT composite powder/precursor processing techniques suggests two methods to be most suitable for uniform dispersion and bonding of CNT with HA. These methods are: (i) chemical precipitation of HA on functionalized CNT and (ii) CVD assisted growth of CNT on HA powder. Apart from the uniform HA precipitation on CNT, chemical precipitation method also ensures good bonding of HA on functionalized CNT surface. Electrostatic attraction of ‘+ve’ charged Ca of HA and ‘−ve’ charged – COOH functionalized group on CNT surface is responsible for this good bonding. In CVD process, the CNTs are individually grown on HA surface, forming a good attachment and dispersion. But, the major problem inherited with both these processes is related to the large scale synthesis of composite powder. Mechanical mixing methods are suitable for bulk production, but are not as good in dispersion as chemical precipitation or CVD. Functionalization of CNTs and use of surfactant help in improving the quality of dispersion in mechanical mixing methods. Spray drying method is a good compromise between large scale synthesis and CNT dispersion but suffers with loss of powder during synthesis. The suitability of all these methods in terms of degree of CNT dispersion is critically discussed in Section 4 of this review. Table 1 presents a summary of all these powder processing routes with their advantages and limitations for HA–CNT system.

3. HA–CNT composite fabrication

Most of the consolidation techniques for fabricating HA–CNT composite uses high temperature, owing to high melting point (1614 °C) of HA [93]. The consolidated HA–CNT composites can be classified into two groups based on the targeted application. They are: (i) free standing composite bodies used as prosthesis or its part and (ii) composite coatings on metallic implants. Researchers have studied different techniques in each of the groups to successfully fabricate HA–CNT composite. Fig. 7 presents a classification of fabrication techniques used to synthesize HA–CNT composites. The main considerations during consolidation are to control the porosity, maintain good dispersion of CNT and at the same time, minimize the chemical dissociation of HA, when exposed to high temperature. Controlling the dissociation of HA to other phases such as tri calcium phosphate (TCP), is required to maintain the mechanical strength of the composite. Controlling the porosity and distribution of CNT is mainly to achieve the good mechanical properties of the composite structure. Though, lowest porosity gives the best mechanical property,

<table>
<thead>
<tr>
<th>Powder processing method</th>
<th>Brief description</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical precipitation</td>
<td>Dispersion of CNTs in a chemical bath and precipitation of HA on its surface</td>
<td>• Uniform HA coating on CNT surface&lt;br&gt;• Improved adhesion between HA and CNT at powder stage</td>
<td>• Not a bulk-scale production route</td>
</tr>
<tr>
<td>Functionalizing</td>
<td>Attaching functional group (e.g. – COOH, – OH and – C=O) on CNT Surface</td>
<td>• Aids in attaching HA to CNT surface at powder stage&lt;br&gt;• Uniform dispersion</td>
<td>• Not a bulk-scale production route&lt;br&gt;• Acid-treatment (functionalization) can damage CNT walls</td>
</tr>
<tr>
<td>Chemical vapor deposition</td>
<td>Growing CNT on HA powder particle surfaces through chemical vapor deposition method</td>
<td>• Dispersion and adhesion of CNT on HA in good&lt;br&gt;• Pristine CNT retains undamaged structure compared to other powder mixing processes</td>
<td>• HA decomposes at high CVD temperature&lt;br&gt;• Metallic catalyst particles get encapsulated in CNT — cytotoxic effect&lt;br&gt;• Process needs to be scaled-up</td>
</tr>
<tr>
<td>Ball milling</td>
<td>Ball milling CNT and HA together to get dispersion of reinforcement phase in matrix phase</td>
<td>• Bulk-scale method for mixing</td>
<td>• CNTs get damaged&lt;br&gt;• Not a very good dispersion — CNT agglomeration is very common&lt;br&gt;• CNTs can get damaged if used excessively</td>
</tr>
<tr>
<td>Ultrasonication</td>
<td>Ultrasonication of CNT and HA together for better dispersion</td>
<td>• Bulk-scale method for mixing&lt;br&gt;• Improves dispersion in conjunction with functionalization or using surfactants</td>
<td>• Chance of agglomeration and non-uniform dispersion without pretreatment of CNTs&lt;br&gt;• May cause problem in final structure if not removed during rapid or low temperature consolidation processes</td>
</tr>
<tr>
<td>Mechanical agitation</td>
<td>Blending of CNT and HA powders together</td>
<td>• Works better with functionalized CNTs</td>
<td></td>
</tr>
<tr>
<td>Surfactant aided dispersion</td>
<td>Adding surfactants to the dispersion medium — one end of surfactants attach to the functionalized CNTs and other end to dispersion medium — causing uniform suspension of CNTs</td>
<td>• Results in uniform dispersion of CNTs when used with methods like mechanical mixing or ultrasonication with dispersion medium</td>
<td></td>
</tr>
<tr>
<td>Spray drying</td>
<td>Atomization of nanosized powders with soluble organic binder to make micron size spherical agglomerates</td>
<td>• Uniform dispersion of CNT in HA nanoparticles&lt;br&gt;• Spherical micron size particles cause easy flow during spraying process and causes uniform composite coating</td>
<td>• Agglomeration of powder particles might not be suitable for attaining high density is some consolidation processes — e.g., pressureless sintering or electrophoretic deposition</td>
</tr>
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</table>
but it is not always desired for orthopedic application. Porosity assists in tissue in-growth and bone integration on implant/prosthesis surface. Hence, the intention of adding CNTs to HA is to improve the mechanical property of the composite, while maintaining some degree of porosity. Following sub-sections deal with the effectiveness of each technique in consolidating HA–CNT composite.

3.1. Free standing HA–CNT composite parts/structures

Conventional powder metallurgy route of powder processing and high temperature consolidation has mainly been applied for fabricating free standing HA–CNT composite, with certain modifications to minimize high temperature exposure for long time.

3.1.1. Sintering

Consolidation of HA–CNT composite by sintering is always performed after green compaction of the powder [50,64,67,72,74,82,94]. Both uniaxial [50,94] and isostatic pressing [82] have been tried for the green compaction. Few studies performed an additional post sintering pressing for better compaction [67,72]. The major concern with conventional sintering of HA is associated with the exposure to high temperature for long time, which causes dissociation of HA to TCP or CaO. A wide range of sintering temperatures starting from 650 °C up to 1200 °C with a dwell time of 2–5 h has been adopted for HA–CNT consolidation. But, temperatures below 1000 °C were not found suitable for achieving sufficient densification. White et al. have reported a density of 63% TD (theoretical density) for HA and 51% TD for HA–CNT when sintered at 800 °C for 2 h [50]. Higher temperature and longer time of heat treatment increase the density and crystallinity of HA [50]. But, sintering at higher temperature increases the chance of dissociation of HA [82,95]. White et al. have also found that the density of HA–CNT composite is lower than HA, when sintered at same conditions [50]. CNTs hold the grains of the matrix apart and thus prevent closure of the porosity. These findings suggest conventional sintering as an unsuitable process for HA–CNT consolidation. Sintering of HA–CNT composites is mostly carried out in vacuum [67,72,74,82] or inert atmosphere, e.g., nitrogen [82] and argon [50,74,82]. An interesting study about the effect of sintering atmosphere on the degree of consolidation for HA–CNT composite has been carried out by Li et al. [82]. Their findings suggest vacuum to be the best sintering atmosphere. Both HA and CNT can absorb gas intensively, which makes the HA–CNT interface bonding weak and increases the porosity content of the sintered structure, when sintered in the presence of any gas. Fig. 8(a) and (b) shows the porous HA–CNT structure sintered in argon compared to its consolidated counterpart sintered in vacuum, respectively. As a result, the composite with same CNT content (3 wt.%) sintered in vacuum offers ~200% more fracture toughness than the one sintered in argon atmosphere [82]. But, a recent study by White et al. [94] has shown a sintering atmosphere, created by bubbling CO and H₂ through cold water bath, to be the best one considering the retention of HA and CNT in the final sintered structure. Sintering atmosphere with a positive pressure of CO and H₂ also can effectively suppress the dissociation of water molecules from HA and its subsequent reaction with CNT [94].

3.1.2. Pressure assisted sintering

In order to overcome HA dissociation and obtain better densification, application of pressure during sintering has been adopted to...
synthesize HA–CNT composites [42,47–49,51,54,60,63,75,90,96]. With application of pressure, densification as high as 96 %TD is achieved at temperature as low as 900 °C [51]. Lower sintering temperature reduces the chance of dissociation of HA. Researchers have also reported sintering at high temperature (1200 °C) with application of pressure, without resulting in dissociation of HA [60,63]. Meng et al. have suggested that application of pressure could inhibit the dehydration of HA even at higher temperature, thus suppressing its dissociation [60,63]. Both uniaxial [49,63] and isostatic hot pressing [47,48,51] with a widely varying pressure range of 28–100 MPa and argon [47–49,51,75] or nitrogen [60,63,90] atmosphere are used to consolidate HA–CNT. Unlike conventional sintering, high pressure sintering in the presence of an inert gas does not create a problem in consolidation and interfacial bonding between HA and CNT. Thus, the mechanical properties of the composite are reported to improve over their HA counterpart, whether it is fracture toughness [51,54,60,90], flexural strength [54,60,90], hardness [51] or compressive strength [42]. The application of pressure might help in driving out the entrapped or absorbed gas on HA and CNT surface and results in lesser porosity in the consolidated product, in contrast to conventional sintering. The

Fig. 9. SEM micrographs of fracture surface for SPS processed HA–CNT composites sintered at (a) 900 °C; (b) 1000 °C; (c) 1100 °C; (d) 1200 °C [87] and (e) high magnification SEM image fracture surface of HA–CNT composite sintered at 1100 °C showing fully densified fine grains structure with CNTs at grain boundary [92].
sintering pressure influences the density of HA–CNT composite, but shows no effect on HA without CNTs. Kobayashi et al. have reported a 10% increase in the relative density of HA–CNT composite when the pressure increases from 7.81 MPa to 15.6 MPa at 1200 °C [75]. They have concluded lower sinterability of the composite in the presence of a second phase.

3.1.3. Spark plasma sintering

Spark plasma sintering (SPS) has also been used to consolidate HA–CNT composites [43,66,76,86–89,91,92]. The advantages of using SPS for HA-based composite are two-fold: (i) retention of fine grain structure and (ii) reduction in HA dissociation. SPS is a very promising technique for processing nanostructured materials, as it retains the fine grain size after sintering [97–101]. It is more attractive for ceramics, as grain size refinement could simultaneously increase hardness and fracture toughness of ceramic due to the deflection of propagating crack and the change of cracking mode from transgranular to intergranular [102]. Requirement of high temperature and longer hold time in conventional sintering causes severe grain growth. Whereas, due to simultaneous application of pressure, electrical current and rapid heating rate, SPS results into better densification of nanoceramic particles in much lower temperature [97–99]. Sintering time for SPS is generally few minutes, compared to few hours in conventional sintering. Due to shorter time of sintering, SPS retains the nanostructure and improves the mechanical property of the sintered body [66,97–101]. In addition, minimal dwell at high temperature causes lesser dissociation of HA into TCP [2,4,5,7,103,104]. SPS of HA–CNT system by our group [92] has revealed the role of CNT in densification and refinement of composite structure. Densification is not very uniform for HA due to its poor thermal (1.25 W/m K) and electrical (7 × 10−7 S cm−1) conductivity [105,106], especially considering the lower sintering time and very fast heating rate in SPS, that cause high thermal gradient across the thickness. High thermal (2980 W/m K) and electrical (1850 S cm−1) conductivity of CNT [107,108] causes uniform sintering and densification throughout the composite structure. Further, grain boundary pinning by CNT also helps in better grain-refinement of the sintered structure [87–92]. Time and pressure of sintering are also found to be the influencing parameters for SPS of HA–CNT system. Similar size of starting powder and SPS temperature with slightly lower pressure (50 MPa) and increased time of ramp heating (5 min) causes a grain size of 25–60 μm [86] compared to submicron grain size (0.6–0.4 μm) with 60 MPa pressure and 3 min ramp time [92]. Increased amount of CNT content (4 wt.%) in reference [92] also causes further grain size refinement by grain boundary pinning than in reference [86] with lower CNT content (1.6 wt.%). Few studies have found that a small amount of HA partially dissolves into β-TCP during SPS processing of HA–CNT composite. Our study has shown the absence of any significant HA dissociation through minimization of SPS cycle time by increasing the ramp heating rate [92]. HA–CNT composites processed through SPS route show an increase in mechanical properties, e.g. fracture toughness [71,86,91,92], elastic modulus [87,92], hardness [86,87,92], bending strength [91] and tribological performance [92]. Thus, SPS is found to be a suitable consolidation process for synthesizing free standing HA–CNT composite parts. The only drawback of SPS with respect to HA–CNT processing is its application of high pressure, which can cause damage to CNT structure and thus have negative effect on the strengthening of the composite. CNTs are reported to collapse or form kinks, caps, onion structure and corrugated walls due to application of pressure during SPS processing [109,110]. SPS of HA–CNT composite at 60 MPa also shows sign of the CNT damage [92].

3.2. CNT reinforced HA coatings

Since the late 1990s, HA is in clinical use as a coating on metallic orthopedic implants [111]. Fig. 10 shows HA coated hip implant parts manufactured by Corin for clinical use. Development of CNT reinforced HA based composite coatings on the metallic substrate is of utmost importance for its projected scope in real life application. The research on synthesis of HA–CNT coatings was started with laser surface alloying and followed up with other techniques, e.g., plasma spraying, electro-photographic deposition and aerosol deposition. The following subsections summarize the significant outcomes of the studies on HA–CNT coating synthesis techniques.

3.2.1. Laser surface alloying

The first HA–CNT composite coating on metallic surface was synthesized by Chen et al. using laser surface alloying (LSA) technique [44]. The high power density applied in LSA acts as a heat sink, causing localized melting of the substrate and forming good adhesion with coating [112]. Thus, it is effective in forming good bonding of ceramic coating on metallic surface. Chen et al. have used Ti–6Al–4V alloy as the substrate for HA–CNT coating [15,44,45]. Ti–6Al–4V is a well-established alloy for orthopedic application and is also in use with HA coating. The substrates were preheated to reduce the residual thermal stress that can cause cracking at interface and delamination of coating. The coating was synthesized using a Nd:YAG laser operating at 400 W power. High

Fig. 10. HA coated orthopedic hip implant parts (http://www.coringroup.com/medical_professionals/products/hips/miniship/).
temperature exposure in LSA causes dissociation of HA to TCP and CaO, which is not favorable for its intended orthopedic application [15,44,90]. Moreover, the Ti alloy substrate gets melted and becomes more prone to react with CNT to form TiC. This phenomenon has two major shortcomings for HA–CNT coating synthesis. Firstly, the presence of TiC in the coating might affect the biocompatibility of the coating, especially when exposed to body fluid and blood stream during wear or dissolution of the HA coating from the implant surface. Secondly, reaction of CNT with Ti will destroy the CNTs and will require increased CNT content to offer required strengthening to HA. But, increase in CNT content results in increased in TiC content also [45]. Though, a portion of CNT reacts with the Ti-alloy substrate, the remaining CNTs were found in the HA coating, maintaining their cylindrical structure [44]. LSA synthesized HA–CNT coating displayed improvement in the elastic modulus, hardness [44,45] and wear resistance [15].

3.2.2. Plasma spraying

In plasma spraying, the micron sized powders are fed through plasma gun and sprayed on preheated substrate to deposit a coating. While passing through the plasma plume, powder particles get exposed to very high temperature (> 10,000 °C) for milliseconds, which causes melting. These molten particles are propelled on the substrate with high velocity to get deformed/flattened through impact and rapidly solidify. Layer by layer deposition of these molten powder particles causes the typical lamellar structure of the plasma sprayed coatings. High temperature exposure in plasma spraying is suitable for preparing ceramic coatings on substrates with good adhesion strength. It is a suitable technique for synthesizing uniform and controlled thickness coating on substrates with complex geometry. Plasma spraying is a US Food and Drug Administration (FDA) approved technique for coating implants with biomaterials [113] and is routinely used for depositing HA coating on implants [114,115]. Thus, plasma spraying is a viable option to synthesize HA–CNT composite coating. In plasma spraying, only powders are exposed to very high temperature and not the substrate. Hence, the chance of TiC formation due to melting of substrate (as in laser surface alloying) does not exist. All studies on plasma spray formed HA–CNT coatings till date have been carried out by our research group [14,32,83–85]. Fig. 11 shows HA and HA–CNT coatings on Ti-6Al–4V substrate deposited using plasma spraying [83]. The cross sectional microstructures of the coatings reveal typical lamellar structure of plasma sprayed coating with uniform thickness. No sign of delamination and cracking at the interface denotes good bonding between the Ti-alloy substrate and HA/HA–CNT coating. Both SEM micrographs of fracture surface and Raman spectrum prove the survival of CNT in the composite coating after being exposed to plasma [32,83]. CNTs survive the high temperature due to the shorter exposure time in plasma (in milliseconds) which prevents their oxidation and destruction. Moreover, ceramic melts during plasma spraying and forms a protective layer on CNTs [116,117]. Powder carrier gas (argon) also creates inert shroud over the particles that shields against oxidation of CNTs. More interestingly, our recent study suggested that the defect density for CNTs decreases after plasma spraying, which could be due to increasing degree of graphitization on CNT walls due to rapid high temperature exposure [32]. X-ray diffraction study on the HA–CNT composite coatings reveals much lower intensity β-TCP peaks compared to peaks from HA phase [83–85]. A negative effect of very fast cooling rate in plasma spraying is decreased crystallinity of HA in the coating. But, the presence of CNT increases the crystallinity of the composite coating, due to its higher heat capacity. A more detailed discussion on this has been presented in Section 4. Similar relative density of both HA and HA–CNT coatings indicates that CNT does not create any problem in densification. Plasma sprayed HA–CNT composite coatings show significant improvement in fracture toughness [32,83–85], hardness [32,74] and wear resistance [14,32,84] compared to the HA coatings. Thus, plasma spraying is an effective technique for synthesizing HA coatings reinforced with CNT.

![Fig. 11. SEM micrographs of coating cross sections synthesized by plasma spraying of (a) HA and (b) HA–CNT [83].](image)

Plasma sprayed coatings generally show lower fracture toughness, elastic modulus and hardness than their sintered/consolidated free standing counterparts. The difference in properties is attributed to the heterogeneity, splats and porosity present in the plasma sprayed structure. One of the prime aims of having plasma sprayed HA based coating on metallic implant surface is to provide an osteo-conductive surface to aid in better bone-integration. The fracture toughness and wear resistance of such coatings should be sufficiently high to maintain its in-vivo integrity [32]. The main load-bearing role in coated implants is played by the tough metal cores. In this context, HA–CNT composite coatings can serve better in keeping the integrity than HA coatings by means of CNT-bridging at the splat–splat and splat–substrate interfaces. CNTs are found to enhance the adhesion of ceramic based single splats on metallic substrate by means of CNT bridging [118].

3.2.3. Electrophoretic deposition

Electrophoretic deposition (EPD) is a colloidal process in ceramic production that is used for preparing cost-effective coatings on substrates with complex geometry. In EPD, charged powder particles, suspended in a liquid medium, are attracted and deposited onto a conductive substrate of opposite charge when DC electric field is applied. It is a widely used coating technique for ceramics [119,120] and is being vastly researched for biomaterials [121] and CNT reinforced composite ceramic coatings [122]. Few studies have been conducted on synthesizing HA–CNT coating for bioimplant surfaces using EPD [57–59,62,78–81,123]. For the effective deposition, the pH of the suspension medium is
maintained in the range of 3.5–5 [58,59,62,78,79]. Applied DC voltage has significant effect on the final coating morphology. A systematic study by Bai et al. shows 20 V to be the optimum voltage to form uniform and continuous coating with no cracks [57]. Increase in the voltage to 40 V causes lot of cracks and porosity in the coating due to significant hydrogen evolution at cathode. Fig. 12 shows the effect of applied DC voltage on EPD coating morphology [57]. HA particles and CNTs are separately added to the suspension with opposite surface charges on them. Thus, they attach to each other to form composite particle, which ensures uniform dispersion of CNT in the composite coating [122]. A low temperature (600–700 °C) post-coating sintering cycle in inert atmosphere is always assisted with EPD to have better densification of the coatings [58,59,62,78]. But, differential shrinkage of coating and substrate during sintering also causes formation of cracks in the coating [62]. EPD synthesized HA–CNT coatings show the absence of delamination and good adhesion with the Ti-alloy substrates [58,62,78]. Increasing CNT content increases the adhesion strength of coating with substrate [58,78]. Incorporation of CNT in HA by EPD is found effective in enhancing the elastic modulus [59], hardness [59] and inter-laminar shear strength [59] of the coating. The main advantage of EPD for synthesizing HA based coating is its room temperature operation followed by a low temperature sintering cycle, which helps in maintaining the crystallinity of HA in the coating [58,78]. Moreover, the absence of high temperature exposure does not create any problem regarding dissociation of HA, which is a problem for most of the other processing techniques [58,78]. But, the major problem with EPD technique is severe cracking of the coating [124], especially with increasing coating thickness. None of the studies on HA–CNT till date has reported synthesizing a coating with >25 μm thickness with insignificant amount of cracks [57,59,62,79]. The presence of cracks deteriorates the mechanical property and strength of the coating and makes it incompatible for the intended orthopedic applications. Fig. 13 presents electrophoretically deposited HA–CNT coatings on Ti alloy, revealing the intensity of cracking with increasing time of deposition [79]. The thickness of the coating in Fig. 13a with 1 min deposition time is reported to be 12 μm. A recent study has shown that addition of TiO2 up to 10 wt.% helps in suppressing the cracks in HA–(5–10)wt.% CNT EPD coatings [123]. Two major contributions by TiO2 in crack inhibition are (i) better comparable (than HA and CNT) thermal expansion coefficient as the Ti-based implant material and (ii) filling up of the cracks and micropores between needle-shaped/elongated HA and CNTs. But, the effect of TiO2 addition on biocompatibility is yet to be established [123], which is critical for the use of this coating in orthopedic applications. Thus, a considerable amount of effort is needed to overcome the problem of cracking in order to have EPD as an efficient technique for synthesizing HA–CNT composite coatings.

3.2.4. Aerosol deposition

Aerosol deposition (AD) uses shock-consolidation principle to form dense and hard coating of fine ceramic powders on metallic, ceramic and plastic surfaces. In AD process, submicron size ceramic particles are accelerated through air/gas flow with a velocity of several hundreds of m/s to collide on the substrate and form a coating. This technique is successfully employed to form ceramic coatings for different applications [125–127]. The only study on synthesizing HA and HA–CNT coating using AD process is conducted by Hahn et al. [61]. A pore and microcrack free HA–CNT composite coating with a uniform thickness of 5 μm is deposited on Ti plate using AD process. CNT addition does not influence the deposition behavior of the coating. HA crystallite size in the coating (5–20 nm) reduces to one tenth of the size in powder stage. Finer crystallite size in coating is due to the fracture of particles during high energy collision with surface, which bonds together in the coating. Low processing temperature of AD process has specific advantage for HA based coating, in maintaining the crystallinity and preventing the HA phase dissociation. Broadening of X-ray diffraction peaks of HA in the coating from the powder stage is due to the fragmentation of crystals in nano-size. But, very low intensity of HA peaks, with respect to that of Ti peaks is not justified, considering the coating thickness of 5 μm. CNT reinforcement in coating is successful in increasing the hardness, but elastic modulus is not improved significantly. The adhesion strength of HA and HA–CNT coatings with Ti substrate remains similar and is claimed to be in the same range of plasma sprayed coatings [61]. Adhesion of ceramic coating with substrate in AD is only due to physical bonding. Considering this fact, an in-depth explanation on the bonding mechanism is needed to justify the reported high adhesion strength, which is absent in the publication [61]. At present, with only one study being done, AD technique is in its infancy to be suggested for HA–CNT coating synthesis. Further studies, addressing the issues
CNT is an added advantage for better consolidating through SPS. Higher thermal and electrical conductivity of CNT helps uniform distribution of thermal energy significantly in very short sintering time of SPS. LSA is an effective method for synthesizing a strongly adherent and dense HA–CNT composite coating. But due to high energy density of laser beam, dissociation of HA and formation of reaction products like TiC occur, which are not suitable for orthopedic application. Plasma spraying is a clinically proven method for HA coating and found suitable for HA–CNT. Plasma spraying of HA might cause dissociation of HA and loss of crystallinity. But addition of CNT in HA does not aggravate its limitations, rather causes improvement in crystallinity. Application of low temperature in electrophoretic deposition and aerosol depositions makes them potential options for HA–CNT coating synthesis. But the major limitation of these processes is the thickness of coating along with the severe cracking. Electrophoretic deposition methods have not been extensively studied for HA or HA–CNT coating synthesis. Table 2 presents a summary of all these consolidation techniques with their main advantages and limitations with respect to HA–CNT system. Effect of composite consolidation techniques on phase transformation and crystallinity of HA–CNT system is addressed in details in Section 4 of this review.

4. Microstructure, phase transformation, and crystallinity of HA composites

Microstructure of the composite revealing the dispersion of CNT in HA matrix is very important for mechanical and tribological performance of the composite. Similarly, phase transformation in HA at high temperature exposure and loss of crystallinity also negatively influence its performance in orthopedic application. Thus, an analysis on role of CNT on these aspects is essential prior to discussing the mechanical and biological performance of the composite.

4.1. Dispersion of CNTs in HA matrix

Uniform distribution of CNTs in the HA matrix is very critical to ensure uniform improvement in mechanical and tribological performance of the composite structure. Agglomeration of CNTs will cause heterogeneous structure leading to poor densification, weak interfacial bonding and stress concentration points in the structure that will aggravate its failure. The natural tendency of agglomeration in CNTs, due to their high aspect-ratio, nano-sized diameter and high surface energy, makes the job of effective dispersion even more challenging. A closer look on the HA–CNT literature reveals that the distribution of CNT in the HA matrix at the powder stage is carried forward in the consolidated structures for both free standing parts and coatings. Uniform distribution of CNTs in spray dried HA agglomerates (Fig. 6) successfully transforms into homogeneous CNT reinforcement in SPS consolidated structure (Fig. 9e) and plasma spayed coating (Fig. 14) [32,92]. Singh et al. have also found that the good distribution of CNTs in HA powder, achieved by ultrasonication (Fig. 5) results into uniform dispersion of CNT in electrophoretically deposited composite coating (Fig. 15) [79]. Chemical precipitation of HA on functionalized CNT helps in uniform mixing of HA and CNT. Bai et al. have reported achieving uniform CNT distribution on electrophoretic coating synthesized using chemically precipitated composite powder in precursor (Fig. 16) [57]. Fig. 17 is the evidence of uniform distribution of CVD grown CNTs on HA in powder and sintered structure [67]. Kobayashi et al. have reported effective dispersion of carbon nano-fiber in HA by ball milling, which is maintained in the hot pressed composite structure (Fig. 18) [75]. Hence, dispersion of CNTs at powder stage is more critical to attain its final homogeneous distribution in the composite.

Dispersion of CNTs in HA at the powder stage has been tried using several techniques, as discussed in Section 2. Most of the studies have used more than one technique simultaneously to achieve the best dispersion. Comparative studies have shown that the degree of CNT dispersion in the composite reveals the dispersion of CNT in HA matrix is very important for mechanical and tribological performance of the composite. Similarly, phase transformation in HA at high temperature exposure and loss of crystallinity also negatively influence its performance in orthopedic application. Thus, an analysis on role of CNT on these aspects is essential prior to discussing the mechanical and biological performance of the composite.
dispersion in HA remains similar for both chemical precipitation and mechanical mixing methods [48,50]. Functionalization of CNTs is effective in enhancing the dispersion of CNT in HA followed by both chemical precipitation and mechanical mixing routes [50]. Forming HA–CNT nano-composite particles in electrophoretic deposition bath using opposite surface charge between HA and CNT is also effective in homogeneous distribution of CNTs in composite coating [122]. But, functionalization using acid treatment poses high chance of damage to CNT’s outer wall(s) which could lead to lowering in the elastic modulus and strength of the composite [42,128], thus defeating the aim of adding CNTs to HA. Similarly, ball milling also generates defects in CNTs and shortens them by breakage, lowering the effectiveness of the reinforcement [128]. Ultrasonication and other mechanical mixing methods could also pose problem if used excessively [128]. Thus, it is very important to assess the damage on CNTs as an effect of powder mixing procedure. CVD is a very useful method for uniform dispersion of CNTs by growing them directly on the surface of ceramic particles such as HA. But, using metallic catalyst particles for CVD growth may create problem at a later stage, due to cytotoxicity related issues. The process proposed by Lu et al. for CVD growth of CNT directly on HA is a suitable solution, though the decomposition of HA in this process needs to be taken care of [68]. Moreover, it is difficult to scale up the CVD process to produce large amount of HA–CNT powder for practical applications. Therefore, it is crucial to develop alternate methods for dispersion of CNT in HA matrix that can overcome the limitations of the existing methods.

Table 2

<table>
<thead>
<tr>
<th>Consolidation method</th>
<th>Brief description</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sintering</td>
<td>Precompaction of composite powder and heating at high temperature in vacuum.</td>
<td>Easy and economic consolidation process</td>
<td>Higher temperature and soaking time cause dissociation</td>
</tr>
<tr>
<td>Pressure assisted sintering</td>
<td>Sintering of powder under high pressure and with a very high heating rate.</td>
<td>Application of very high pressure reduces HA dissociation</td>
<td>Long soaking time might lead to grain growth</td>
</tr>
<tr>
<td>Spark plasma sintering</td>
<td>Sintering of powder under high pressure and pulsed current with very high heating rate.</td>
<td>Very rapid sintering process reduces chance of HA dissociation.</td>
<td>Very small exposure at high temperature helps retaining nano-structure.</td>
</tr>
<tr>
<td>Laser surface alloying</td>
<td>Laser assisted pulsed melting and fusion on metallic substrate to form coating.</td>
<td>Forms strong and adherent coating</td>
<td>Dissociation of HA due to high energy density laser beam exposure.</td>
</tr>
<tr>
<td>Plasma spray forming</td>
<td>Composite powder is fed through plasma gun and sprayed on substrates</td>
<td>Suitable for uniform dispersion of CNTs in HA matrix</td>
<td>Chance of dissociation of HA matrix - Though addition of CNT reduces the risk of dissociation.</td>
</tr>
<tr>
<td>Electrospinning</td>
<td>Composite powder is extruded through a spinner and sprayed on substrates.</td>
<td>Uniform dispersion of CNT in HA matrix</td>
<td>Chance of dissociation of HA matrix - Though addition of CNT reduces the risk of dissociation.</td>
</tr>
<tr>
<td>Aerosol deposition</td>
<td>Composite powder particles are charged, and sprayed on conductive substrates.</td>
<td>Uniform dispersion of CNT in HA matrix</td>
<td>Not studied thoroughly - Adherence could be an issue.</td>
</tr>
</tbody>
</table>

Fig. 14. SEM micrograph of the fracture surface of plasma sprayed HA–CNT coating showing uniform distribution of CNT in HA matrix.

Fig. 15. SEM micrograph of electrophoretically deposited HA–CNT coating suggesting good dispersion of CNT in HA [79].
application. Spray drying is a suitable process for dispersing CNTs in HA at large scale. But micron sized powder agglomerates might not be suitable for all the composite solidification/fabrication processes to achieve the required density of the structure, e.g. normal sintering without application of pressure or electrophoretic deposition. Hence, an optimum powder processing method is required for the effective CNT dispersion at powder-mixing and consolidation stages.

4.2. Phase transformation and crystallinity of HA matrix in composite

One of the main concerns regarding high temperature processing of HA is the loss of hydroxyl group to form oxyapatite and oxyhydroxyapatite, which starts at 900 °C in air and 850 °C in water free atmosphere [129–131]. Further dissociation of HA at higher temperatures (1200–1450 °C) is very much sensitive to the Ca/P ratio, which is 1.67. In case of Ca/P< 1.67, HA dissociates into β-TCP (α-TCP at higher temperature) and tetra calcium phosphate (TCP). HA dissociates to CaO when Ca/P > 1.67 [3,131]. The dissociation of HA into TCP or other phases has two major effects on the consolidated structure. Firstly, the dissociated phase causes problem in densification and significantly lowers the strength of the structure [131,132]. Secondly, the phases formed by dissociation of HA lead to considerable increase of the dissolution rate in physiological pH, as confirmed by the in-vitro tests [133]. Dissociation of HA inside a living body is unsuitable for orthopedic applications. Similar problems also exist for HA–CNT composite system. Moreover, H2O formed due to dehydroxylation of HA at higher temperature can also react with CNT to cause damage to nanotubes.

HA dissociation does not exist for synthesis routes that employ lower temperature, e.g. electrophoretic and aerosol deposition of coatings [58,61,78]. Electrophoretic deposition generally requires a post-sintering treatment. But, the sintering temperature (600–700 °C) is lower than the HA dissociation start temperature (850–900 °C). The problem regarding phase transformation of HA is largely associated with the high temperature synthesis routes. Conventional sintering of HA–CNT composite leads to HA dissociation [49,82]. Phase dissociation is mainly detected by analysis of X-ray diffraction (XRD) pattern of the composite structure. JCPDS PDF No. 9-432 is used for the detection of characteristic diffraction peaks from HA. The presence of dissociated phases is also detected by referring to JCPDS data-base, e.g., PDF No. 9-169 for β-TCP, PDF no. 29-359 for α-TCP etc. The reference XRD data for CNT is available in JCPDS PDF No. 23-0064 for graphite. CVD growth of CNTs on HA powder also introduces transformation phases in the composite powder [68]. The study by Li et al. reveals the effect of CNT in increasing dissociation of HA during sintering at 1200 °C [82]. Sintering of pure HA produces β-TCP at 1200 °C. But, the presence of CNT causes further decomposition of HA into α-TCP and γ-Ca3P2O7.

![Fig. 16. SEM image of electrophoretically deposited HA–CNT coating from chemically precipitated composite powder [57]. The arrows indicate dispersed CNTs.](image1)

![Fig. 17. SEM images of uniformly distributed CNT in (a) CVD processed composite powder and (b) sintered composite fracture surface [67]. The white arrows indicate uniformly distributed protruded CNTs on fracture surface.](image2)

![Fig. 18. Fracture surface of sintered HA–carbon nano-fiber composite showing the uniform distribution of reinforcement phase [75].](image3)
which requires higher heat input. High specific heat of CNTs [134] can enable them to work as heat sink and assist in further dissociation of HA in the neighboring region. A recent study by White et al. suggests that combination of water, CO, and H₂ is an ideal sintering atmosphere for HA–CNT [94]. The presence of carbon monoxide and hydrogen in atmosphere shifts the equilibrium of reaction between H₂O and C, and thus retains CNT and prevents dehydroxylation of HA. Application of pressure during sintering is found effective in partially suppressing dissociation of HA in most HA–CNT systems [47, 60, 63]. Meng et al. have suggested that application of pressure could reduce the dehydration and decomposition of HA [63].

In this regard, rapid processing routes such as SPS or plasma spraying become attractive. The faster synthesis time can reduce the dissociation of HA to some extent by defeating the kinetics of the phase transformation reactions. SPS processed HA–CNT systems show partial decomposition of HA into a very small amount of β-TCP in the sintered structure [76, 87]. Faster heating rate with the decreased time of SPS can even result in total suppression of HA dissociation to any significant amount, as observed by our research group [92]. Kalmadia et al. have reported the presence of β-TCP in their SPS sintered HA–18.4 wt.% Al₂O₃–1.6 wt.% CNT composite structure even at a higher heating rate [86]. But, closer observation of the XRD pattern (Fig. 19) presented in the same study reveals that 100% intensity peak of β-TCP (2θ = 30.9°) is not present in the pure HA sample, whereas it is present in other two samples containing Al₂O₃ and Al₂O₃+ CNT respectively. As all three samples were sintered using same SPS parameters, the dissociation of HA in the composite cannot be attributed solely to sintering. Though not reported by the authors of the same study [86], the dissociation of HA could be due to Al₂O₃. Previous studies have shown the effect of Al₂O₃ on increasing dissociation of HA at high temperature exposure [135, 136]. Plasma spray forming of HA–4 wt.% CNT composite coating also reveals minimal dissociation of HA to form a small amount of β-TCP, which is evident from the very low intensity of the TCP peaks compared to much higher HA peaks [83]. However, laser surface alloyed HA–(5/10/20 wt. %) CNT composite coatings show very significant amount of HA dissociation [44]. Melting of the substrate along with the coating material during laser surface alloying exposes HA to high temperature for longer duration as compared to plasma spraying, and hence results in its dissociation. None of these rapid processing routes reports increase in HA dissociation in the presence of CNT. Higher specific heat of CNTs might not induce significant effect due to faster consolidation time for SPS and plasma spraying, as it does in case of conventional sintering. One important issue, while discussing the phase dissociation of HA in HA–CNT system, is the solubility or diffusion of carbon atoms in HA lattice. But, no report is available on the diffusion of C in HA lattice and corresponding change in HA cell volume. On the contrary, Rietveld analysis of the neutron diffraction data by Keally et al. indicates no change in the structural parameter (cell constant) of HA in HA–2 wt.% CNT system sintered up to 1000 °C [47]. No other report is available through Raman spectroscopy or FTIR analysis, which confirms reaction between HA and CNT or any reaction phase formation.

Crystallinity of HA is another important variable as it influences the mechanical properties. The presence of amorphous phases increases the dissolution/resorption rate of HA, which is not suitable for its intended orthopedic applications [137, 138]. Amorphization of HA is not a concern for most of the synthesis processes used in consolidation of HA–CNT composites, except plasma spraying, which involves extremely high cooling rates, in the range of 10⁵–10⁷ °C s⁻¹. A study by Keally et al. on hot pressing of HA–2 wt.% CNT composite has shown a fully crystalline HA consolidated structure with no significant effect of CNT addition on the unit cell parameters [47]. Another study by the same group has reported an increase in the crystallite size of HA with 5 wt.% CNT addition [49]. But the crystallite size was found to be decreasing for higher CNT content (12 and 25 wt.%). The initial increase in HA crystallite size could be due to higher specific heat and thermal conductivity of CNT, which provides more heat to neighboring regions aiding in grain growth. But, with increasing CNT content, pinning action offered by CNTs at grain boundaries becomes dominating to reduce the crystallite size. Inhomogeneous distribution of CNTs in the reported structure is also responsible for such behavior [51]. White et al. have also reported increasing crystallinity in HA–5 wt.% CNT composite system with increasing sintering temperature [50]. As mentioned earlier, formation of amorphous phases is a concern in HA coatings synthesized using plasma spraying. But, addition of CNTs is found to act as a solution of this problem. Balani et al. reported that plasma sprayed HA–CNT coating shows significantly increased crystallinity (80.4%) compared to HA coating (53.7%) synthesized using the same parameters (Fig. 20a) [83]. Increased crystallinity in HA–4 wt.% CNT system is attributed to higher thermal conductivity of CNTs compared to HA, which helps in nucleation and precipitation.

![X-ray diffraction pattern of SPS sintered HA](image1)

![X-ray diffraction pattern of plasma sprayed HA coatings](image2)
of HA. Higher heat capacity of CNT can absorb more heat when exposed to the plasma and then higher thermal conductivity of CNT can create a thermal pool around while cooling. Both of these phenomena provide an enhanced cooling time to the HA matrix in the neighboring region of CNTs, which helps in its recrystallization. SEM image presented in Fig. 20b shows the evidence of nucleation and precipitation of fine HA crystals on CNTs during plasma spraying [32]. Another study by Tercero et al. on plasma sprayed HA–18.4 wt.% Al₂O₃–1.6 wt.% CNT coating, provides further evidence on effect of CNT in increased crystallinity of HA based composite coating [85]. Both the HA and HA–Al₂O₃ coatings show same type of amorphous hump in the XRD pattern, whereas, sharp crystalline HA peaks with reduced amorphous hump are observed with the CNT addition. It can be inferred from these observations that Al₂O₃ does not contribute toward the crystallinity of HA composite coating due to its poor thermal conductivity. Thus, the presence of CNTs tends to improve the crystallinity of HA in composite systems.

5. Mechanical properties of HA–CNT composite

The main aim of CNT addition to HA is to improve the overall mechanical properties of the composite. CNT is found effective in increasing the fracture toughness, elastic modulus, hardness and bending strength of HA–CNT free standing parts and coatings. HA–CNT interface is very important in dictating the mechanical performance of the composite system. Another important consideration for composite coating is its adhesion strength with the substrate. Researchers have studied the effect of CNT addition on adhesion strength of HA based coating with underlying titanium substrate [58,59,61,78]. The following subsections present a comprehensive summary of the effect of CNT addition on the fracture toughness, elastic modulus, hardness, strength and tribological performance of the composite.

5.1. HA–CNT interface: bonding and strength

In addition to homogeneous dispersion of CNTs in HA matrix, the interfacial bonding between HA and CNT is another necessary condition for improving the mechanical and tribological performance of the composite. Both HA and CNT are non-reacting inert phases in their pure state. Some studies have used functionalized CNTs to chemically attach HA on their surface (refer to Section 2.1.2). Chemical attachment of HA on CNT surface is supposed to offer good interfacial strength in composite structure. But, the related studies have just mentioned about the interfacial strength of HA–CNT in composite without an attempt to analyze or quantify it. Though, many of the studies have presented a visual proof of good HA–CNT interfacial bonding through high magnification SEM images of fracture surface as shown in Figs. 17b and 21 [32,60,61,92]. Reinforced CNTs protruding from the HA matrix with no cracks or gaps visible at the interface represent a good interfacial bonding.

Keally et al. used synchrotron radiation diffraction data from HA–(5–25 wt.%) CNT samples to predict the microstrain present in the hot pressed composite [49]. Introduction of CNTs in HA matrix is found to introduce microstrain in the HA matrix. The increase in strain by 0.007% with increasing CNT content up to 25 wt.% indicates a degree of bonding between HA and CNT. Our research group has quantified the interfacial strength of HA–4 wt.% CNT bond in the SPS processed composite [92]. High resolution TEM analysis at the interface reveals the lattice orientation relationship between the CNT and adjacent HA crystal (Fig. 22). HA crystals on the CNT surface and its open ends, try to align themselves to generate a minimal lattice strain, resulting in coherent or semi-coherent interfaces. Coherency at the interface improves work of adhesion and thus, contributes toward good interfacial bonding. In the same study, CNT pull out energy from HA matrix was quantified using the model developed by Chen et al. for ceramic–CNT
The calculated CNT pull out energy (1.5–22 J/m²) was found to be greater than the fracture energy of monolithic HA (1 J/m² [140]), which indicates a very strong bonding between HA and CNT in the SPS structure.

The nature of HA–CNT interface bond depends on the synthesis route of the composite. For example, it would be interesting to study the bonding nature and strength of chemically bonded HA–CNT interface, formed through precipitation of HA on functionalized CNTs. The knowledge of interface will help in developing the HA–CNT system with optimized mechanical and tribological properties and would ensure its prolonged performance in real life application.

5.2. Fracture toughness

Bones are the load bearing parts of a living body. Thus, they need to possess good fracture toughness (KIC) to prevent cracking and fracture on the application of high and cyclic loading during limb movement and actions. Fracture toughness of dense HA (1 MPa.m0.5) is significantly lower than the minimum reported value for cortical bone (2 MPa.m0.5) [3]. Thus, to replace bone as an implant or coating, fracture toughness of HA needs to be improved. CNTs have been explored as a second phase reinforcement for improving the fracture toughness of HA based composite parts and coatings. The role of CNT in improving the fracture toughness of the composite system can be explained using three main toughening mechanisms — (1) crack deflection; (2) CNT pull-out and (3) crack bridging.

(1) Crack Deflection: When a crack propagates through the matrix and reaches a CNT across its path, the crack gets deflected and absorbs some energy resulting in toughening of the matrix. Chen et al. have developed an analytical model to predict the deflection of crack and energy release rate due to the deflection for ceramic–CNT composite system [139]. Studies on HA–CNT system mention about crack deflection as one of the toughening mechanism contributing toward higher KIC of composite than only HA [60,63,90].

(2) CNT Pull-out: Pulling out of CNTs from the ceramic matrix can dissipate energy due to binding and friction and subsequently, leads to toughening. Figs. 17b and 21 show SEM images of CNT pull-out from the fracture surfaces of HA–CNT composite matrix, reported in different studies [32,60,67,75,76,84,85,92,96,127].

(3) Crack Bridging: CNTs can act as bridges and restrict the widening of the cracks. CNT bridges require more energy for opening up of the cracks and cause toughening. Our research group has calculated the HA–CNT bonding energy to be higher than the fracture energy of monolithic HA [92]. Thus, the crack propagating through HA gets restricted when it comes in the vicinity of CNT, as more energy is required for CNT debonding. Fig. 23 presents CNT bridging in SPS processed HA–CNT composite. Other studies have also shown evidence of CNT bridging as an effective mechanism for the toughening of HA–CNT composite structure [32,60,63,83,86].

Most of the studies have used indentation based technique for the measurement of fracture toughness. Fig. 24 shows a comparison of the published data on the percentage improvement in the fracture toughness as a function of CNT content in the composite. The value of KIC in each study depends on several factors including processing route, powder morphology, structure type — i.e. free standing or coating. Thus, the percentage improvement of KIC in HA–CNT system is calculated with reference to KIC of the HA structure (without CNT) reported in the same study. A few studies have adopted Al2O3 or ZrO2 in addition to
CNT, which also contribute toward toughening of the HA matrix [63, 84–86]. In those cases, the comparison has been made between the two compositions having HA–Al2O3/ZrO2 and HA–Al2O3/ZrO2–CNT. The CNT content in Fig. 24 is presented in weight percentage. In cases where CNT content is reported as volume percentage, it is converted to weight percentage using the density of HA and CNT as 3.2 g/cm³ and 2.1 g/cm³ respectively. The improvements are classified in terms of the consolidation routes to comprehend if any significant trend in fracture toughness is expressed (Fig. 24). In general, SPS processed composites show an increase in the fracture toughness with CNT content. Plasma sprayed coatings show 56 and 369% improvement in KIC with similar CNT content (4 wt.%) in two different studies [32, 83]. But, the different results are attributed to two powder processing routes. Lower improvement (56%) is achieved in case of mechanically mixed powder [83]. Spray drying of HA–CNT powder led to the 369% improvement in KIC in plasma sprayed coating [32] due to homogenous CNT dispersion. Sintering route does not show any trend in fracture toughness improvement as a function of CNT content. Pressure assisted sintering also does not show any trend with CNT content, though fracture toughness enhancement is maximum at low CNT content (3 wt.%) and deteriorates further, probably due to agglomeration of the reinforcement phase. A detailed case-wise analysis and comparison of KIC improvement, presented in following paragraphs of this section, reveal different features/aspects of HA–CNT composite that influence the fracture toughness.

The highest improvement in KIC of ~650% is obtained by Li et al. with 3 wt.% CNT addition [82]. HA was sintered in air, whereas, the HA–3 wt.% CNT system that shows maximum improvement in KIC was sintered in vacuum. This study has also mentioned that sintering in the presence of any gas is detrimental for HA based system. HA surface can absorb gas that deteriorates its densification and sintering in vacuum produces best densification. Thus, 650% improvement in KIC in this study is a cumulative effect of CNT reinforcement and better densification in absence of gas. On closer observation of other studies that have shown more than 100% improvement in KIC, the effect of uniform dispersion of CNT becomes more evident. CVD grown CNTs on HA powder by Li et al. ensure good dispersion at powder and consolidated stage. A 225% improvement in fracture toughness was observed with only 2 wt.% CNTs grown via CVD [67, 72]. The surface adsorption force at CVD grown CNT and HA particles interface plays an important role in the high performance of the composite. Spray drying assisted uniform dispersion of CNTs in HA helps in improvement of KIC by ~92% and ~350% in HA–CNT composite synthesized by SPS and plasma spraying respectively [32, 92]. Using the powder with similar CNT content (4 wt.%) and dispersion causes different improvements in KIC for SPS and plasma sprayed structures, which could be attributed to the specific consolidation routes [32, 92]. The degree of heterogeneity in microstructure is much more in case of plasma sprayed structure, with the presence of pores, unmelted particles, intersplat cracks and weak regions. SPS processed structures are much more homogeneous in comparison with plasma sprayed coatings. Thus, the KIC of plasma sprayed HA structure is much lesser than SPS processed HA structure.

Lower increase in KIC can be associated with the existence of agglomerated CNTs in the sintered structures, due to poor CNT dispersion at the powder stage [51, 60, 76]. Meng et al. have provided a direct evidence of effect of CNT dispersion on KIC of hot pressed HA–CNT composite [90]. Better dispersion of CNT with similar content (3 wt.%) is reported to increase KIC by 5%. Another study by Meng et al. on optimization of CNT content in hot pressed composite has shown that 7 vol.% (~4.7 wt.%) CNT addition causes the maximum improvement in KIC, as presented in Fig. 25 [60]. Further increase in CNT content causes agglomeration and deterioration of fracture toughness. Similar observation is reported by Lei et al. also, with 3 wt.% CNT showing the best improvement in fracture toughness (260%) in hot pressed composite [54]. The credit for such impressive improvement is attributed to dispersant assisted uniform distribution of CNT in HA matrix. The studies, which have used an additional reinforcement phase (Al2O3 or ZrO2) than CNT, show relatively lower degree of KIC improvement due to CNTs [61, 79, 80]. KIC of HA in those cases is already improved significantly with the Al2O3 or ZrO2, leaving less room for improvement by CNT.

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addition. The only study that shows agglomeration of CNT and still higher improvement in $K_{IC} (-130\%)$ is by Tanaka et al. on SPS processed HA–6 wt.% CNT system [91]. But, the study does not provide a suitable justification for such behavior, contradictory to all other studies on HA–CNT systems. Tanaka et al. have very briefly mentioned about anisotropic nature of CNT clumps that can prevent grain boundary cracking from extension. But, CNT clumps are supposed to create a very weak interface with HA matrix, which could have severe detrimental effect on the toughness of the composite. Sintering temperature in SPS processing is also found to have direct effect on the fracture toughness of the HA–CNT composite. Sarkar et al. have reported fracture toughness of HA–2.5 vol.% (1.65 wt.%) CNT synthesized by spark plasma sintering at 1000, 1100 and 1200 °C [76]. Lower temperature (1000 °C) leaves significant porosity, whereas higher temperature (1200 °C) results in excessive grain growth. As a result, transgranular type of fracture with easily propagating cracks dominates in both the cases; having deteriorating effect on the fracture toughness. HA–CNT composite sintered at 1100 °C shows fine grained consolidated structure. Intergranular fracture with CNT pull-outs is prevalent in this structure, which absorbs energy while cracks propagate and increase the fracture toughness [76,87]. Moreover, the fine grained structure, generated due to grain boundary pinning action of CNT, is also effective in increasing the fracture toughness of the composite structure [92,102].

The dispersion of CNT in HA matrix and densification are two most critical factors for improvement of fracture toughness in HA–CNT system. Comprehensive outcomes of all the studies indicate that ≤ 5 wt.% CNT is effective for improvement in fracture toughness, irrespective of the processing technique. Agglomeration of CNTs at higher content is responsible for deterioration in $K_{IC}$. CNT improves the $K_{IC}$ of composite by absorbing the dissociation energy, crack deflection, and crack bridging in HA matrix. CNT induced toughening is highly effective even in porous and heterogeneous structures such as plasma sprayed HA coatings, indicating dominance of toughening effect over porosity. Densification of the composite is found to be more sensitive to the processing parameters than CNT content, when CNTs are homogeneously dispersed [50,82]. The fracture toughness of the composite decreases with increasing porosity content [82] and thus from mechanical integrity point of view, densification is desirable for HA–CNT composites. But, integration of the neobone on implant requires in-growth of bone tissues [141–144], which is favored by the open porosity exposed on the implant surface. Thus, for HA–CNT composites, the most desirable structure should be one with densified core, free from closed porosities for mechanical support and open, interconnected micro-porosities at the outer region near surface for bone integration. For HA–CNT coated metallic implants, a porous coating with fracture toughness (> 2 MPa.m^{0.5} [3]) and shear strength (35 MPa [78]) in the range of cortical bone should be an excellent one.

5.3. Elastic modulus

Elastic modulus (E) of human cortical bone is reported to be in the range of 15–25 GPa [145,146], whereas it is much higher (~100 GPa) for consolidated monolithic HA [147,148]. Mismatch of E at bone–implant interface might pose a risk of fracture or delamination of implant. But, osseointegration ability of HA creates a strong bonding at HA–bone interface, which reduces the chance of delamination and fracture. Thus, unlike fracture toughness, elastic modulus of HA need not be improved to match with bone. But, increase in E directly influences improvement in the fracture toughness in ceramic based composite systems. Fracture toughness of brittle ceramic system is mainly estimated from indentation cracking using Anstis’ equation [149], median crack equation by Lawn [150] or Evans’ relationship [151] as follows:

\[
\text{Anstis’ Equation: } K_{IC} = 0.016 \left( \frac{E}{H} \right)^{0.5} \frac{P}{c^{2.5}} 
\]

\[
\text{Evans and Charles Equation: } K_{IC} = 0.16 \frac{E}{H} a^{0.5} \left( \frac{c}{a} \right)^{-1.5}. \text{Where } c/a \geq 3
\]

Expression (3) was later modified with a non-dimensional factor (E/H)^0.5 [152], where, $K_{IC} =$ is the fracture toughness, E – is the elastic modulus, H – is the hardness, a – is the half diagonal length of indent and c – is the radial crack length.

The studies on HA–CNT systems have used above-listed three equations for determining the fracture toughness [32,60,67,76,83–85,92]. It is clear that an increase in E is beneficial for the increased fracture toughness, which is essential for application of HA–CNT for orthopedic applications.

Improvement of elastic modulus in HA–CNT system is due to the high elastic modulus of CNT (200–1000 GPa [25]) and good bonding at HA–CNT interface. Upon application of a stress on HA–CNT, the matrix starts deforming first due to its lower elastic modulus. If the HA matrix has a strong interfacial bonding with much stiffer CNTs, then effective transfer of stress can take place from matrix to the reinforcement. CNTs can absorb much more stress than HA to produce similar amount of the elastic strain. Thus, the resultant elastic strain generated in the composite structure is reduced compared to HA for the same applied stress, resulting in increased effective elastic modulus for HA–CNT. SPS processed HA–4 wt.% CNT structure is found to possess E value [92] that is in reasonable agreement with the predictions by micromechanical models of Esheleby [153] and Mori–Tanaka [154]. A cross-linking model for estimating the Young’s modulus of HA-functionalized CNT composite proposed by Saffar et al., shows that the improvement in modulus of the composite depends on the CNT content, its aspect ratio, number of cross links and characteristics of interfacial reaction [155]. Cross links are the points where HA attaches to functionalized sites on CNT surfaces, and are considered as active load transfer points through HA–CNT interface during modeling.

Comparative analysis of the HA–CNT literature data reveals no improvement in E for CNT content beyond 4–5 wt.% [32,44,45,51,59,61,83,84,86,87,92]. All the studies have used nanoindentation technique to measure the elastic modulus for HA–CNT, from the slope of the unloading curve using the Oliver–Pharr method [156]. Most of the studies have reported the increase in E up to 70% with CNT content varying in a range of 1.3–12.5 wt%. Homogeneous dispersion of CNTs and good HA–CNT interfacial bonding play key role in increasing E of the composite [32,44,59,87,92]. On the contrary, agglomerated CNTs with weak interfacial bonding reduce the elastic modulus of the composite as compared with pure HA [51,86]. Keally et al. have reported 2% decrease in E with increasing CNT content, which is attributed toward agglomeration of CNT in the structure [51]. Whereas, Kalmodia et al. have found weak interface, yielding easier sliding in nano-scale length, to be responsible for a 22% decrease of E after 1.6 wt.% CNT reinforcement [86]. Our research group has found an increase in the fraction of the elastic work with CNT addition in SPS processed structure, which makes the matrix more prone to recovery upon deformation [92]. Improvement in E for plasma sprayed HA–4 wt.% CNT coating (73%) is slightly at the higher side [32]. It is a combined effect of strengthening offered by CNT reinforcement and increase in crystallinity due to presence of CNT, as discussed in Section 4 [83].

Similar to $K_{IC}$, optimum sintering temperature is found to have a direct relationship with E of the SPS processed HA–2 vol.% (1.3 wt.%) CNT structure [87]. The E of composite sintered at 1100 °C shows the best improvement. Both lower and higher temperatures of sintering cause reduction in E due to poor consolidation and excessive grain growth respectively. Lower E at higher consolidation temperature could also be due to possible damage in CNT structure [87].
The only study that has reported a very impressive increase in $E$ with CNT addition is by Kaya for electrophoretically deposited HA coatings [59]. Addition of 1 and 2 wt.% CNT increases $E$ of the composite coating by 82% and 108% respectively, when compared with HA coating. No detailed explanation has been provided for such a huge increase in $E$. But, the $E$ value reported for the HA coating is significantly low (15 GPa), as compared to other studies, which report $E$ of pure HA in the 50–150 GPa range [32,45]. The study on electrophoretically deposited HA–CNT coatings did not provide details of the indentation experiments or load vs. displacement curves to better understand such an impressive improvement.

CNTs show significant effect on the improvement of elastic modulus ($E$) for HA–CNT composite, which has a direct positive influence on $K_C$ of the structure. The degree of dispersion of CNTs and bonding at HA–CNT interface are two critical factors that govern $E$ of the composite system. Similar to fracture toughness, the elastic modulus improvement of HA–CNT system is most effective at $\leq 5$ wt.% CNT content as it reduces agglomeration of nanotubes (Fig. 26).

5.4. Hardness

Addition of CNT also influences the hardness for HA based composite. The higher stiffness of CNT provides a strengthening effect in HA matrix, which causes hindrance to plastic deformation. Instrumented indentation has always recorded lower penetration depth with similar load application in HA–CNT compared to HA [44,45,84,92]. Significant decrease in pile up at the edge of nano-indent with increasing CNT content is a direct evidence of higher resistance to plastic deformation [45]. The presence of CNT is found to decrease the fraction of plastic work and increase the depth of elastic recovery upon release of load [92]. Grain boundary pinning and refinement of structure by CNT also help in simultaneous increase in hardness and fracture toughness [71,87,92,102].

Researchers have used Vicker's hardness measurement [32,76,86,92] and instrumented nanoindentation technique [44,45,51,59,61,66,84,87,92] to quantify hardness of HA–CNT composite. Based on this comparative data, addition of CNT beyond 4–5 wt.% is found ineffective in terms of hardness improvement of the composite structure [32,44,45,51,59,61,66,84,86,87,92]. Comparatively higher increase in hardness is noted for composite coatings processed by laser surface alloying [44,45], plasma spraying [32] and electrophoretic deposition [59]. In case of laser surface alloyed HA–CNT coatings on Ti–6Al–4V substrate, formation of TiC ceramic adds to the overall hardness [45]. Plasma sprayed HA–4 wt.% CNT coating displays 87% improvement in hardness as compared to HA coating [32]. Electrophoretically deposited HA–CNT coating shows very high improvement in hardness of 287% and 647% with 1 and 2 wt.% CNT addition respectively [59]. An $H$ value of 36.44 GPa with 2 wt.% CNT addition has been reported, which is very high. The same study has also reported high $E$ value (178 GPa) measured through nanoindentation study. No adequate explanation has been provided for such extraordinary improvement in the mechanical properties. Similar to elastic modulus, agglomeration and weak interface cause lower increase and/or decrease in hardness with CNT addition. Researchers have observed decrease (18–8%) in $H$ with 10–12.5 wt.% CNT addition, which is due to the agglomeration of CNT into SPS and hot pressed composites [51,66]. A 28% decrease in $H$ with 1.6 wt.% CNT addition to HA–Al$_2$O$_3$ (18.4 wt.%) system is recorded by Kalmadia et al., which has been attributed to the incomplete densification of the structure in presence of CNT [86]. Higher consolidation temperature (1200 °C) can also have adverse effect on hardness, due to possible damage and destruction of CNT structure, as reported by Xu et al. [87]. But the study by Sarkar et al. [76] has contradicted the findings by Xu et al. [87] in terms of hardness of SPS processed HA–CNT composite. The former one reports gradual increase in hardness with sintering temperature up to 1200 °C, in spite of grain coarsening at that temperature [76]. Though, no further explanation has been provided.

Addition of CNT improves the hardness of HA impressively due to (i) strengthening of matrix and (ii) grain size refinement — both of which hinder plastic deformation. Agglomeration of CNT in HA matrix is detrimental to hardness improvement. Similar to $E$, the hardness of composite structure is also dependent on the processing parameters of consolidation method.

5.5. Strength (flexural and compressive)

Strength of HA–CNT system is measured mostly in tensile mode using flexural or bending strength [54,60,63,67,72,75,82,90,91] with only one study on compressive strength [42]. Bending strength has been measured for sintered [67,72,82], hot pressed [42,54,60,63,75,90] and SPS processed [85] free standing composite using three point [54,63,91] or four point [75] bending tests. Strengthening of HA–CNT composite structure is governed by two major factors; (i) dispersion of CNTs; (ii) bonding at HA–CNT interface. Homogeneous dispersion of CNTs helps in the uniform distribution of stress in the structure and hence, uniform strengthening. The agglomeration of CNTs causes stress concentration points and non-uniform distribution of stress. Moreover, the interface of HA and agglomerated CNTs being weak acts as source of failure under stress. Li and co-workers have shown broken and pulled out CNTs on the fracture surface of sintered composite, indicating that CNTs can share significant portion of load transmitted from the HA matrix [67,72]. They have reported 49% increase in bending strength with 2 wt.% CNT addition and attributed it to uniform dispersion of CVD grown CNTs on HA and good interfacial bonding. Other studies have also shown similar improvement in bending strength with 3–4 wt.% CNT addition in HA [54,75,91]. Meng et al. have presented the bending strength of hot pressed HA–CNT composite as a function of CNT content (Fig. 26) [60]. This systematic study on optimization of CNT content shows a maximum bending strength achieved with 7 vol.% (5 wt.%) CNT. The bending strength of the composite decreases with larger CNT content, as CNT tends to agglomerate. The highest improvement in bending strength of HA–CNT (164%) is reported by Li et al. with 3 wt.% CNT addition [82]. But, the sintering condition for HA and HA–CNT being different, the properties cannot be compared directly.

The only study that reports compressive strength of HA–CNT composite is by Zhao and Gao on hot pressed structure [42]. HA–2 wt.% CNT possesses a compressive strength of 102 MPa, which is a 61% improvement over HA. It was also concluded that chemically modified CNTs result in more effective bonding with HA and results in 23% more compressive strength as compared to unmodified CNTs in HA–CNT composite.
Reinforcement of CNTs in HA improves the strength of matrix, whether it is tensile (flexural) or compressive. The improvement in strength is dependent on dispersion of CNT and bonding at HA–CNT interface. Decrease in the bending strength of composite with higher CNT content (> 5 wt.%) occurs due to agglomeration of nanotubes. Direct dependence of composite strength on the interface bonding becomes more explicit with chemically modified CNT reinforced composite showing better compressive strength than unmodified nanotube reinforcement.

5.6. Adhesion strength of HA–CNT coating with substrate

Adhesion strength of HA based coating with the metallic implant surface is important for determining the life cycle in orthopedic application. Weak coating–substrate interface can cause premature and easy failure and peeling off inside the living body, thus defeating the purpose of having HA coating on metallic implants. Reports are available on the adhesion strength of electrophoretically deposited and aerosol processed HA–CNT coatings with the Ti-alloy substrate [58,59,61,78]. There is no study on direct measurement of adhesion strength of HA–CNT composite coatings synthesized by laser surface alloying and plasma spraying.

Adhesion strength has been estimated in terms of shear stress required to delaminate the HA–CNT coating from the Ti-alloy substrate. Fig. 27 presents a schematic diagram of the testing set-up that is used in a tensile testing machine by Lin et al. for measuring the adhesion strength [78]. All the other studies have followed the same principle and similar set-up. Kaya et al. have reported very low adhesion strength of 2.8 MPa for electrophoretically deposited HA–2 wt.% CNT coating on Ti–6Al–4V alloy substrate [58,59]. But, the reported increase in adhesion strength of HA with 2 wt.% CNT addition is a very impressive amount of 300%. Lin et al. have achieved much higher adhesion strength of HA (20.62 MPa) and HA–20 wt.% CNT (34.94 MPa) coating electrophoretically deposited on Ti substrate [78]. One of the reasons for an increase in the adhesion strength with CNT addition is the anchoring between the coating and substrate by CNTs, as observed by Kaya et al. (Fig. 28) [62]. Bridging by CNTs inhibits the detachment of coating from the substrate on the application of a shear force. Long time post sintering can also result in diffusion assisted bonding in electrophoretically deposited coatings.

No data is available on laser surface alloyed HA–CNT coating with Ti substrate. But, the coating process itself is potential enough to ensure good metallurgical bonding at interface [157,158]. In laser surface alloying, a thin layer of Ti substrate is melted which serves as the matrix for HA–CNT powder to form a composite coating. Plasma spraying is the most potential technique for synthesizing HA–CNT coating as it is a US Food and Drug Administration (FDA) approved process for depositing HA coatings for orthopedic applications. However, no report is available on the adhesion strength measurement for plasma sprayed HA–CNT coating. Though several studies have reported the adhesion strength of plasma sprayed HA/HA-based composite coatings on the Ti-alloy substrate. The adhesion strength has been measured to be 25–40 MPa [159–161]. High temperature exposure in plasma spraying causes partial melting of HA powders, which causes good bonding with the substrate after a high velocity impact. However, formation of a good bond between the coating and substrate is highly dependent on the large number of processing variables associated with the plasma spraying process.

HA–CNT coatings, synthesized by other methods have also reported coating/substrate adhesion strength. Hahn et al. have reported good adhesion strength (~30 MPa) for aerosol deposited HA–(1–3 wt.%) CNT coatings [61] comparable to electrophoretic deposited and plasma sprayed coatings. Though, no significant difference in adhesion strength is observed for coatings with and without CNTs. Good bonding in aerosol deposited coating is attributed to the mechanical impact of powder particles propelled on substrate surface with very high velocity of several hundred m/s [61,125]. Aerosol deposition of ceramic powder is similar in mechanism to cold spraying of metallic powders [162]. In case of metallic powders, the bond strength of cold sprayed coatings with substrate is dominated by the plastic deformation of powder particles that helps in adhesion between coating and substrate. But, due to the brittle nature of ceramics, plastic deformation might not be large enough in HA. Thus, further explanation is needed to justify the good adhesion strength of aerosol deposited HA coatings.

It should be noted that shear strength of natural cortical bone is reported to be 35 MPa [78], which is similar to the adhesion strength between Ti substrate and HA–CNT coatings, synthesized using different techniques. Hence, HA–CNT coatings are suitable for orthopedic application with respect to their adhesion strength with metallic implant surfaces. Addition of CNT helps increasing the adhesion of electrophoretically deposited HA coatings, by providing anchoring between coating and the substrate. Aerosol deposited coating does not indicate any such role played by CNT to improve the adhesion. But, anchoring by CNT can possibly play an important role in adhesion of laser surface alloyed and plasma sprayed coatings. Formation of TiC in case of LSA also influences adhesion strength of the coating. In case of plasma sprayed coatings, higher heat content of CNT is beneficial for better spreading and mechanical interlocking of the coating with substrate.

5.7. Tribological behavior

Poor wear resistance of HA is one of the shortcomings for its application as orthopedic implant [3–5,14,15]. Poor fracture toughness causes low wear resistance of HA. Wear volume loss is a combined
function of the elastic modulus, hardness and fracture toughness of ceramics. A model by Evans and Marshall for estimation of the wear volume in brittle ceramic shows dependence of the wear resistance on the mechanical properties as follows [163]:

\[ V = P^{1.125} K_{IC}^{-0.5} H^{-0.25} \left( \frac{E}{H} \right)^{0.8} S \]  

where, \( V \) is the wear volume, \( P \) is the normal load, and \( S \) is the total traveling distance on wear track.

One of the main objectives for adding CNT in HA is to improve its wear resistance. A few studies have reported the effect on CNT addition on the wear resistance of HA–CNT composite and coatings [14,15,32,84,92]. These studies have investigated a variety of issues such as wear at macro and nano-scale lengths, in dry and physiological condition and also with varying CNT contents. Macro-scale wear studies are mainly carried out using ball-on-disk [32,92] or pin-on-disk [14] methods, whereas nano-scale wear studies are carried out by performing nano-scratches using nanoindenter [15,84,92]. The outcomes of all the studies have merged in to a common agreement that CNT reinforcement improves the wear resistance of HA in any environment (wet or dry) at macro, micro and nano-scale lengths.

The macro-scale wear study on SPS processed HA–CNT composite reveals 60% decrease in coefficient of friction (CoF) and 66% increase in wear resistance with 4 wt.% CNT addition [92]. The decrease in CoF is due to peeling of graphene walls from CNTs by shear force applied during wear. These peeled off graphene sheets offer more lubrication in the wear track. Fig. 29 shows the presence of damaged and broken CNTs observed in the wear track. Evidence of increasing defect density from the relative intensity of D and G peaks (of CNT) in Raman spectrum also supports the peeling of graphene layers during wear [92]. The increasing wear resistance in the HA–CNT structure is reported to be a combined effect of increasing fracture toughness and decreasing CoF. On the contrary, nano-scale wear study shows increase in CoF with CNT addition [92]. Such differential behavior in macro and nano-wear is justified by the force experienced in the two modes [92]. Unlike macro-wear, the shear force applied in nano-wear is not large enough to peel off graphene layer from CNT surface. Thus, the absence of lubrication along with increasing strength and fracture toughness of composite structure causes increase in CoF for nano-wear. The increase in wear resistance (45%) is also less in nano-wear due to the absence of contribution from the reduced CoF.

Our research group has also conducted macro-scale wear study of plasma sprayed HA–4 wt.% CNT coating on the Ti-alloy substrate, using parameters simulated with the movement of human acetabular cup during walk [32]. Addition of 4 wt.% CNT decreases the CoF by 25% (Fig. 30). Wear volume is also reported to decrease by 80% and is evident from the optical profile of wear tracks on HA and HA–CNT coatings presented in Fig. 31. The reason for decreasing CoF and improved wear resistance in HA–CNT coating is similar to that of SPS structure, as discussed in previous paragraph. The presence of CNTs also controls the wear mechanism and wears debris size distribution. The wear in HA–CNT is reported to be dominated by abrasion, whereas, it is mainly chipping and fracture dominated wear only in HA due to its poor fracture toughness [32]. Wear particles consist of a large size variation and larger particles in the absence of CNTs. Size of wear particle is very important due to its differential cytotoxic effect inside the living body. Cytotoxic effect of wear debris with respect to particle size and the presence of CNT are explained later in Section 6.1.5.

Balani et al. have performed nano-scale wear study on plasma sprayed HA based coating reinforced with both 18.4 wt.% aluminum oxide and 1.6 wt.% CNTs [84]. The comparison of properties has been carried out for the two compositions having HA + Al₂O₃ and HA + Al₂O₃ + CNT, in order to separate out the reinforcing effect from CNT only. CNT reinforcement has not posed any significant effect on CoF of the coatings, as observed in Fig. 32. This study further proves the absence of peeled off graphene layer in the wear track, due to small amount of shear force in nano-scratch. The improvement in the wear resistance is 80% with only 1.6 wt.% CNT addition, which is very significant when compared with the macro-scale wear study in the plasma sprayed coating with 4 wt.% CNT [32]. Thus, the trend of wear resistance at different scale lengths in plasma spraying is opposite to that in SPS, i.e., more wear resistance at nano-scale length. These results can be explained in terms of plasma sprayed coating's microstructure. Though lubrication from CNT is absent in nano-wear track, still its depth is confined in a single splat, which is a very dense and almost monolithic structure. On the other hand, depth of macro wear track is several microns, which covers a very heterogeneous region with multiple

![Fig. 29. SEM micrographs of broken and damaged CNTs observed in the wear track of SPS processed HA–CNT composite [92].](image-url)
splats and inter-splat regions. Weak inter-splat regions with cracks, porosities and few unmelted particles cause significant decrease in the wear resistance at macro-scale. Thus, the final percentage improvement in wear resistance at macro-scale length is resultant of increase in wear resistance due to graphene aided lubrication and decrease due to heterogeneous structure. So, in case of plasma sprayed coating, the effect of CNT is more obvious for nano-scale wear and gets partially ciphered at macro-scale.

Balani et al. have also studied the wear resistance of HA–4 wt.% CNT coating immersed in simulated body fluid (SBF) and concluded that CNT reinforcement improves the wear resistance [14]. Nano-scale wear study on laser surface alloyed HA–(5–20 wt.%) CNT coatings by Chen et al. reports lower depth of scratch, indicating increased wear resistance due to graphene aided lubrication and decrease due to heterogeneous structure. So, in case of plasma sprayed coating, the effect of CNT is more obvious for nano-scale wear and gets partially ciphered at macro-scale.

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Table 3
Summary of biocompatibility studies on HA–CNT composite systems.

<table>
<thead>
<tr>
<th>HA–CNT composition/processing</th>
<th>Type of bio-study</th>
<th>Details of the study</th>
<th>Major findings</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 wt.% CNT – Hot Pressing</td>
<td>Immersion in SBF</td>
<td>• Immersed in SBF for 3, 10 and 17 days</td>
<td>• Apatite growth rate is lower in first few days – afterwards becomes higher – composite is claimed to have high bioactivity</td>
<td>[90]</td>
</tr>
<tr>
<td>4 wt.% CNT – Plasma Spraying</td>
<td>Cultured osteoblast cells on coatings – SEM</td>
<td>• Human osteoblasts were cultured on coatings for 3 days • Cells were fixed and observed under SEM</td>
<td>• Human osteoblasts grow on HA–CNT surface – alongside CNTs • HA can precipitate on CNT surface</td>
<td>[83]</td>
</tr>
<tr>
<td>3 wt.% CNT – Cold Compaction and Sintering</td>
<td>In-vivo – embedded in striated mouse muscle</td>
<td>• The cylindrical composite samples were embedded into striated mouse muscle • The mice were sacrificed at 1, 3, 5, 7 and 14 days • The tissues around were observed under microscope</td>
<td>• Initially some immune activity is observed — inflammatory cell infiltration, blood vessel dilation, lymphocyte infiltration and monocyte production is observed • At 14 days the inflammatory reactions are reduced • No necrosis of tissue occurs • The nearby tissue remains normal</td>
<td>[82]</td>
</tr>
<tr>
<td>20 wt.% CNT, Electrophoretic Deposition</td>
<td>Osteoblast like MG63 cell culture on coating</td>
<td>• Cells cultured on composite coatings for 3 days • Cells were cultured till they reached 90% confluence</td>
<td>• Most of the protein shows similar expression on substrates.</td>
<td>[78]</td>
</tr>
<tr>
<td>2 vol.% CNT – Spark Plasma Sintering</td>
<td>Protein profile of osteoblast cultured on composite surface using iTRQ-coupled 2D LC MS/MS Analysis</td>
<td>• Cells were cultured till they reached 90% confluence • Cells were lysed and extracted protein was quantified • Antibodies were used to detect different proteins • Cells were also fixed for SEM study</td>
<td>• Upregulation of Foutin A is observed in case of both HA and HA–CNT – which is associated with suppressed calcification. • Relatively high EF2 level was detected in HA–CNT than in HA – which participate in the elongation phase during protein biosynthesis on the ribosome • CNT slightly promote the protein expression and cytoskeleton protein distribution • Major cytoskeletal proteins slightly decreased level on HA–CNT than HA – denotes less adhesion on surface • For metabolic enzymes – related to osteoblast proliferation – some shows increased and some of the decreased level on HA–CNT compared to HA • EF2 shows higher level on HA–CNT – responsible for accelerated Ca²⁺ dissolution from composite surface</td>
<td>[88]</td>
</tr>
<tr>
<td>2 vol.% CNT – Spark Plasma Sintering</td>
<td>Protein profile of osteoblast cultured on composite surface using iTRQ-coupled 2D LC MS/MS Analysis</td>
<td>• Cells were cultured till they reached 90% confluence in 4 days • Cells were lysed and extracted protein was quantified • Antibodies were used to detect different proteins • Cells were also fixed for SEM study</td>
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<td></td>
</tr>
<tr>
<td>HA–1 wt.% and 3 wt.% composite coating on Ti – Aerosol Deposition</td>
<td>Cytotoxicity, Differentiation by ALP activity and SEM of pre-osteoblast cells (MC3T3-E1)</td>
<td>• SEM of cells fixed after 5 h of incubation • Cytotoxicity assessed using LDH Assay after 24 h of incubation • Cell Differentiation evaluated by measuring ALP activity of cells cultured on coatings for 10 days</td>
<td>• Cells on HA–CNT surface spreads better and has longer flaps than on HA and bare Ti surface • HA–CNT surface shows lower cytotoxicity than HA and Bare Ti • Morphology of fixed cells reveal normal attachment on all the coatings</td>
<td>[61]</td>
</tr>
<tr>
<td>HA–Al₂O₃–1.6 wt.% CNT composite coating on Ti-alloy – Plasma Spraying</td>
<td>Osteoblast quantification and SEM observation</td>
<td>• Cells were fixed and observed in SEM after 3 days of culture • Cells were counted using hemocytometer after 1, 3 and 7 days of culture</td>
<td>• HA–CNT surface shows better proliferation and significantly higher ALP Activity than HA and Ti</td>
<td>[85]</td>
</tr>
<tr>
<td>HA–2 vol.% CNT – Spark Plasma Sintering</td>
<td>Osteoblast quantification and SEM observation</td>
<td>• Cells were fixed and observed in SEM after 1 Days of culture • Cells were counted using hemocytometer after 2 and 4 Days of culture</td>
<td>• Number of cells was higher on HA–CNT than on HA.</td>
<td>[87]</td>
</tr>
<tr>
<td>HA–CNT composite – prepared by chemical precipitation method – were dip coated from solution on glassy carbon electrode – hemoglobin was deposited by immersing in its phosphate buffer solution</td>
<td>Application as biosensor and bioelectrocatalyst</td>
<td>• Biosensor capability studied by amperometric response to H₂O₂</td>
<td>• HA–CNT–Hb shows fast amperometric response</td>
<td>[56]</td>
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</tr>
<tr>
<td>HA–ZrO₂–3 wt.% CNT — Hot Pressing</td>
<td>SBF Immersion</td>
<td>• Immersion of composite in SBF for 10 days</td>
<td>• Needle like apatite crystal precipitates on composite surface</td>
<td>[63]</td>
</tr>
<tr>
<td>HA–CNT — Electrophoretic Deposition</td>
<td>MTT assay and SEM observation on mouse Osteoblasts (MC3T3-E1)</td>
<td>• Cells were fixed and observed in SEM after 2 days of culture</td>
<td>• Thickness of apatite layer increases with time</td>
<td>[57]</td>
</tr>
<tr>
<td>HA–Al₂O₃–1.6 wt.% CNT — Spark Plasma Sintering</td>
<td>MTT assay and SEM observation on mouse Fibroblasts (L529)</td>
<td>• Cells were fixed and observed in SEM after 3 days of culture</td>
<td>• Fibroblast viability on HA–Al₂O₃–CNT surface remains similar to HA in 3 days, but decreases after 5 days.</td>
<td>[86]</td>
</tr>
<tr>
<td>HA–4 wt.% CNT — Plasma Spraying</td>
<td>Viability study by Fluorescent staining in human osteoblasts; Cytotoxicity of wear debris to osteoblasts and macrophages</td>
<td>• The viability of osteoblasts was evaluated using fluorescent staining (FDA-PI) on the coatings — after culturing for 3, 5 and 10 days.</td>
<td>• Fibroblast viability on HA–Al₂O₃ is minimum for both 3 days and 5 days</td>
<td>[32]</td>
</tr>
<tr>
<td>HA–2 wt.% CNT (CVD grown on HA) — Sintering</td>
<td>Viability Study by MTT Assay on L529 mouse fibroblasts</td>
<td>• MTT assay was performed after culturing the cells on HA–CNT for 2, 24, 48, 72, 96 h</td>
<td>• The viability is increased by 75% at 2 h and increases to 100% later</td>
<td>[72]</td>
</tr>
<tr>
<td>HA–4 wt.% CNT — Plasma Spraying</td>
<td>In-vivo biocompatibility and evaluation of mechanical integration at bone–implant interface using rat model</td>
<td>• The coated titanium implants were implanted in rat — which was sacrificed after one month</td>
<td>• Histological studies indicated no inflammatory reaction at HA–CNT interface</td>
<td>[180]</td>
</tr>
<tr>
<td>HA–4 wt.% CNT — Plasma Spraying</td>
<td>Quantifying adhesion strength of osteoblast on implant surface and studying actin expression to understand the biological mechanism of CNT-induced adhesion</td>
<td>• Osteoblast cells grown on coated titanium implant</td>
<td>• CNT is found increasing the adhesion energy of osteoblast cells on HA surface</td>
<td>[183]</td>
</tr>
</tbody>
</table>
for laser surface alloyed coating is higher than the others (SPS and PSF) by an order of magnitude. Higher load (up to 100 mN) employed by Chen et al. has the potential to cause graphene peeling and thus increased lubrication in HA–CNT wear track [15].

Improvement in the wear resistance of HA–CNT system is the result of the dual role played by CNT, viz. (i) improved fracture toughness of HA, which causes removal of mass difficult and, (ii) lubrication through peeled graphene layers from CNT walls, which reduces the effective lateral force. The benefits of CNT reinforcement in improving the wear resistance vary across the nano and micro scale-length due to difference in interaction volume and amount of CNTs in that volume. The wear of HA–CNT can result in formation of CNT containing debris, which may have significance on its biocompatibility. The role of CNT containing wear debris on the biocompatibility is discussed in following section.

6. Biocompatibility of HA–CNT composite

HA–CNT composite systems are intended for orthopedic application in a living body. Hence, it is extremely important to assess their biocompatibility, by means of in-vitro and in-vivo studies, before suggesting their clinical use. HA is already a clinically proven biomaterial and is used as coating for metallic implants. But, the biocompatibility of CNT is still under debate [36]. Several studies have been carried out to study the cytotoxicity of carbon nanotubes since 2001 [30,35–37,164–169]. The topic remains controversial till date with contradictory reports by different search groups [35,37,164,166,167]. For example, Cherukuri et al. have reported that CNTs can be ingested by macrophages without producing any toxic effect [164]. But, Cheng et al. have reported frustrated/incomplete phagocytosis of CNT in macrophages, causing oxidative stress and cell death [167]. A recent study by Kagan et al. reveals ingestion and biodegradation of carbon nanotube by human macrophages and neutrophils without any inflammatory or toxic response [35]. Comprehensive reviews on this issue have agreed that the reported cytotoxic response of CNT is mostly not due to CNT itself, but is associated with the impurities and catalyst particles, degree of agglomeration, surface defects and also on the effect of cell culture medium, secondary chemicals, and pH values [36–38,165]. Thus, Ren et al. have suggested standardization of the assessment method to comment on the cytotoxic effect of carbon nanotube on the cells, organ, or whole organism [37]. While considering the application of HA–CNT composite in orthopedic implants, there is at least three major points in favor. Firstly, CNTs have cytotoxic effect mainly when they are suspended in fluid medium, while they appear nontoxic if immobilized to a matrix or to a culture dish [38]. Secondly, there are several reports of CNTs having positive response to bones and bone cells. Usui et al. have found that CNTs show good bone–tissue compatibility without any toxic effect [30]. CNTs, when implanted with collagen in a mouse skull, aid in accelerated bone growth [30]. Bone forming cells (osteoblasts and fibroblasts) show normal growth and proliferation on CNTs [31,39,40,170]. Fig. 33 shows fibroblast cells grown on vertically aligned carbon nanotubes [40]. Recent studies have reported increased proliferation and adhesion of osteoblast cells on CNT or graphene based surfaces, due to the selective absorption and attachment of proteins from cell culture medium by means of non-covalent C–C bonds [33,34,171,172]. Osteoblast cells are reported to attach better on CNT coated collagen surface than collagen, which is the main component of natural bone and widely used in orthopedic scaffolds [41]. Thirdly, if the CNTs are released in the blood stream along with the wear debris generated from the composite surface, they are either biodegraded completely by neutrophils and macrophages [35] or safely cleared out from the body by renal excretion route very quickly, without causing toxic effect in any organ [166,173]. Hence the use of CNT in HA based composite should not have negative impact on the biocompatibility. The precipitation of HA on the CNT surface (Fig. 20b) adds to the biocompatibility by offering better integration with the newly formed bone [32,83]. Several reports are available on apatite formation ability of CNT-surface, when immersed in simulated body fluid [174–179]. Still, a thorough investigation of the biocompatibility of HA–CNT composites, prepared by different techniques, is mandatory for the clinical application. Several research groups have carried out different types of in-vitro biocompatibility assessments for HA–CNT composites, whereas, only two reports are available on in-vivo study [82,180]. Table 3 summarizes the biocompatibility studies with the brief description of methodology, cell-lines, assessment techniques used and the major outcomes. The following subsections briefly present the important outcomes of the biocompatibility studies with possible explanations of results and their significance in orthopedic biocompatibility of HA–CNT system.

6.1. In-vitro assessment of biocompatibility

In-vitro biocompatibility studies are generally carried out by growing bone cells (osteoblasts, fibroblasts) on HA–CNT composite surface or by SBF-immersion of the composite to study the apatite formation.

6.1.1. Osteoblast/fibroblast proliferation and viability

The very first study on growing of osteoblast cells on plasma sprayed HA–4 wt.% CNT coating surface was carried out by Balani et al. [83]. SEM image of fixed osteoblast cells reveals good spreading on CNT reinforced HA surface. Few other studies have also reported proliferation and attachment of osteoblast cells on HA–20 wt.% CNT composite surface [73]. The presence of CNTs in HA is reported to improve bone cell proliferation [57,61,87,89]. Fluorescence micrographs in Fig. 34 show increasing number of osteoblasts on HA–4 wt.% CNT surface than HA, when cultured for 3, 5 and 10 days. Viability assessment also shows increasing percentage of live cells in the presence of CNT [32,57,72,86]. Liang et al. have reported increasing viability of fibroblasts with incubation time on HA–CNT surface up to 100% in 4 days [72]. Osteoblasts attach better on HA surface in the presence of CNT, as seen in Fig. 35 [61]. The cell on HA–3 wt.% CNT surface has formed several filipods to get attached after 5 h of seeding, whereas the cell on HA surface still maintains the globular shape and is yet to spread out (Fig. 35). Lee et al. have also reported active spreading of osteoblasts on HA–CNT surface with several filopodia protrusions [181]. Higher ALP (alkaline phosphatase) activity for osteoblasts on HA–CNT surface denotes increasing differentiation [61]. Several factors are claimed to cause better proliferation and viability of osteoblast on HA–CNT composite surface, viz. (1) attachment of proteins on the surface from the cell culture medium [32]; (2) the special porous structure and high surface area of CNT [78]; (3) higher porosity content in HA–CNT composite [86] and (4) bioactive nature of CNT [80,81]. HA–18.4 wt.% Al2O3–1.6 wt.% CNT composites prepared by plasma spraying and SPS also show similar trend of osteoblast proliferation and viability [85,86]. Minimum osteoblast proliferation and viability is noted for HA–20 wt.% Al2O3 surface and it increases with CNT addition. But both these composites show lesser proliferation and viability than HA. It seems that bio-inertness of Al2O3 poses a negative effect on the osteoblast behavior. At the same time, addition of CNTs plays a positive role in reviving the proliferation of osteoblast on the composite surface. Increased roughness in the composite coating structure is also reported as a cause of delayed proliferation of osteoblast [85].

6.1.2. Protein profile study of osteoblasts

Ji et al. have studied the profile of cytoskeletal proteins, metabolic enzymes, signaling proteins and cell growth proteins that regulate osteoblast cell growth and proliferation on HA and HA–2 vol.% (1.3 wt.%) CNT surfaces [88,89]. Cytoskeletal proteins show higher expression on HA than HA–CNT surface, which means better osteoblast cell adhesion on HA. This observation contradicts the SEM image of fixed cells by Hahn et al. (Fig. 35) that shows better osteoblast attachment in HA–3 wt.% CNT surface [61]. Further studies are
needed to resolve the contradiction between the direct visualization of cell growth and protein profile results. Metabolic enzymes involved in the cell proliferation show higher expression on HA–CNT surface, suggesting enhanced osteoblast proliferation in the presence of CNTs. This observation is supported by an increased cell density count on HA–CNT than HA [89]. Analysis of signaling and cell growth proteins shows higher expression of EF-2 (elongation factor-2) on HA–CNT surface, which indicates accelerated dissolution of Ca$^{2+}$ from surface. On the contrary, Narita et al. have shown that CNTs inhibit osteoclast proliferation and reduce the apatite resorption [182]. Thus HA–CNT surface has the potential to make a balance for dissolution of calcium ion from the implant surface.

### 6.1.3. Quantifying adhesion of osteoblasts

Osseointegration ability is very crucial for orthopedic surfaces, which will determine the life-time of the implants. Adhesion of bone cells on implant surface plays an important role in osseointegration. Adhesion of osteoblast is generally assessed indirectly by retention of cells on HA–CNT surface. But, a recent study from the present authors has quantified the adhesion of osteoblasts on HA–CNT surfaces at single cell level [183]. A nano-scratch based technique was applied to determine the lateral force and energy required to detach a single cell on HA–CNT coated surface as compared to plasma sprayed HA coating. Fig. 36(a) presents the bar-chart showing comparative adhesion energy of a single osteoblast on HA and HA–CNT surfaces for different days of incubation. HA–CNT surfaces are reported to show 73, 95 and 63% higher adhesion energy than HA for 1, 3 and 5 days of incubation, respectively. Staining of the actin network reveals more spreading of osteoblast in presence of CNT (Fig. 36b) and develops an insight into the integrin mediated adhesion mechanism of osteoblast on surfaces containing CNT.

### 6.1.4. Immersion in simulated body fluid

Apatite precipitation ability of any surface during SBF immersion is a preliminary indicator of its capability to get integrated with new bone in-vivo. The suitability of SBF immersion test as an indicator of biocompatibility could be best justified through a statement made by Kokubo.
6.1.5. Cytotoxicity of HA–CNT wear debris

Wear debris is generated from the implant surface during its service period. This debris interacts with bone cells (osteoblasts) in surrounding regions. Also, in the long run, the debris is carried through body fluid and may be introduced in the blood stream. Once in the blood stream, the wear debris is first attacked by the macrophages, phagocytosed and cleared out from the body. Hence, it is very important to check the cytotoxic effect of the CNT containing HA debris for both osteoblasts and macrophages. Our research group has used lactate dehydrogenase (LDH) assay to determine the cytotoxic effect of HA and HA–4 wt.% CNT wear debris on osteoblasts and macrophages [32]. The wear debris, collected from the ball-on-disc wear tests were mixed with the cell culture medium. Osteoblast and macrophages were cultured in that medium for 3 days before the cytotoxicity assay. Osteoblasts show lesser cytotoxic response to HA–CNT debris with more % living cell with HA–CNT wear debris is correlated with the smaller size of the debris particles that are easy for phagocytosis and the presence of CNT that increases osteoblast proliferation. Macrophages shows similar cytotoxic response to both HA and HA–CNT debris. The outcome of this study emphasizes similar biocompatibility of HA wear debris with or without CNT.

In-vitro biocompatibility studies for HA–CNT composite have revealed compatible and positive role of CNT toward proliferation, viability, attachment, differentiation, apatite formation and cytotoxicity in most of the cases. The only report on protein profile analysis of osteoblasts, cultures on HA–CNT surface, contradicts all other in-vitro studies in issues related to osteoblast attachment and calcium dissolution (refer to Section 6.1.2). This demands further follow-ups on protein profile analysis of osteoblasts on HA–CNT surface to confirm and explain the results. Apatite formation ability from body fluid indicates the suitability of HA–CNT implant surface to get integrated with new bone. The issue of wear debris related cytotoxicity is also addressed by checking cytotoxicity of CNT containing HA wear debris with osteoblasts and macrophages. In-vitro studies carried out till date on HA–CNT systems can claim the presence of CNT in HA to be biocompatible; in fact advantageous in some aspects.

6.2. In-vivo assessment of biocompatibility

There are only two in-vivo studies on HA–CNT system [82,180]. Though the first one is not a real bone–implant, but sintered HA–CNT composite was embedded in a striated rat muscle [82]. The big white rats were sacrificed in 1, 3, 5, 7 and 14 days to assess the histocompatibility of HA–CNT composite. The striated muscle after 1 day shows little inflammatory cells and lymphocyte infiltration. The inflammatory cell infiltration increases in day 3 with sign of blood vessel dilatation. Both of these phenomena increase gradually on 5 and 7 days. But, after 14 days, the inflammatory cell infiltration decreases significantly and mild dilatation is observed. The muscle tissues after 14 days look similar to natural undamaged tissue, which indicates recovery [82].
The second study used plasma-sprayed HA–CNT coated titanium rods as implant in femur of rats [180]. HA coated and uncoated implants were used as control groups. The rats were sacrificed after one month to retrieve the implants. The implants were found well positioned with no infected tissues around after one month of in-vivo exposure. TEM analysis of neobone at implant surface showed the restoration of normal trabecular bone and bone marrow without inflammatory reaction on HA–CNT surface (Fig. 37a), similar to HA and Ti surfaces. Dynamic mechanical analysis at bone–implant interface revealed the distribution of elastic modulus across interface. HA–CNT and HA coated surfaces lead to smoother transition of elastic modulus across bone–implant interface as compared to bare-Ti surface with a sharp gradient (Fig. 37b). Increasing modulus gradient across interface possesses the risk of fracture and delamination at bone–implant interface. In addition, the presence of CNT in HA is found causing accelerated bone growth and mineralization. This study presents the first indication of in-vivo non-toxicity for HA–CNT composite and its positive influences on bone growth [180]. Further studies are needed by implanting HA–CNT composites in bones for longer time period, to establish its absolute in-vivo biocompatibility. The analysis of outcomes from all these in-vivo studies would be able to predict the suitability of HA–CNT for clinical use in orthopedic implants.

7. Future direction and strategies

The review of literature indicates an increasing amount of the research in exploring HA–CNT system for orthopedic application. The effect of CNT reinforcement in strengthening of HA based composite system has been much in focus; though biocompatibility still remains a topic of debate. Several powder processing routes have been used for the dispersion of CNT in HA matrix. Processes like chemical precipitation, CVD, functionalization of CNT and spray drying have shown promise in effective dispersion of CNT. Spark plasma sintering for composite and plasma spraying for coatings are found to be the promising consolidation methods for HA–CNT. A good insight has been developed on the phase transformation and crystallinity of composite. CNT reinforcement is effective in increasing the fracture toughness, elastic modulus, hardness and flexural strength of the composite. Distribution of CNTs in HA matrix is found very crucial for mechanical strengthening of the composite structure. Few studies have also established the positive influence of CNT reinforcement on the adhesion of composite coating to the metallic implant surface. Biocompatibility of HA–CNT composites has been studied to some extent in terms of in-vitro assessment and very less in in-vivo. The present scenario of development suggests following directions, which need attention and more research for successful clinical application of HA–CNT system in orthopedics.

• Uniform dispersion of CNT in HA is very important and is best achieved by chemical precipitation or CVD method. But the slow production rate is a major limitation for scaling-up in these two techniques. Composite powders with high CNT to HA ratio could be produced by chemical precipitation or CVD method. This powder could be mixed with more HA powder using mechanical mixing to adjust the final CNT content, which is much lower. This strategy could help in scaling up the production of composite powder. Studies are required to ensure the dispersion ability of such adopted composite powder preparation techniques. Quantifying dispersion of CNTs in HA as a function of processing route would further help in assessing the best process route.

• Electrophoretic and aerosol deposition techniques are excellent options for HA–CNT composite coating preparation due to lower thermal exposure that eradicates the HA dissociation and crystallinity related problems. But both these methods have limitations regarding thickness of coating and severe cracking. More research is needed to overcome these problems associated with electrophoretic and aerosol deposition techniques.

• High temperature dissociation of HA in HA–CNT system is critical for orthopedic applications. Though it has been addressed by few researchers, a clear understanding of the CNT’s role in dissociation of HA at different temperatures, time of thermal exposure and environment of consolidation is missing. Future research should entail the effect of consolidation methods on phase transformation of HA–CNT system during processing.

• Knowledge about HA–CNT interface is vital in determining the mechanical and tribological performance of the composite. But, very little and insufficient information is available about HA–CNT interface. More studies are required to understand the type of interface and the bond strength between HA and CNT as a function of different processing techniques. This knowledge would be helpful in determining the best processing route to achieve the expected strengthening of the composite structure.

• It is important for HA–CNT coatings to achieve good adhesion with substrate for practical application. But, no study exists on adhesion of HA–CNT coating for plasma sprayed coatings, which is the FDA approved coating synthesis method for HA. Few studies on electrophoretic and aerosol deposition evaluate the adhesion strength of HA–CNT coating with substrate. But, only one study has tried to analyze the role of CNT on adhesion of coating, in terms of anchor [62]. The role of CNT in adhesion of HA composite coating to the underlying substrate needs to be addressed in detail.

• Tribological behavior of bio-implant surfaces is very important for their in-vivo exposure. Wear resistance of HA based coating increases significantly with CNT addition, due to the dual role played by CNT. Few studies performed till date on this issue reveal great dependence of tribological behavior on microstructure of the composite, which is governed by the consolidation method. Thus, more research is required on tribological behavior of differently processed HA–CNT composite to fully understand the advantage/disadvantage of CNT reinforcement in HA. Further, biological fate of the wear debris generated is of great concern, considering in-vivo implantation of the composite structure. Till date, only one study addresses the cytotoxicity of CNT containing wear debris with osteoblasts and macrophages [32]. The analysis of this study reveals the dependence of cytotoxicity on size of wear debris, which is a function of composition and consolidation of the composite. Understanding the wear behavior of differently processed HA–CNT composite and the fate of wear generated debris under biological conditions is an interesting research area which is yet to be explored fully.

• In-vitro biocompatibility studies, performed by culturing bone cells on HA–CNT surface, prove its biocompatibility in terms of proliferation, viability and differentiation. But, the only report on protein profile analysis of osteoblasts contradicts other results to some extent. Thus, thorough protein profile analysis of bone cells on HA–CNT surface is required to prove the biocompatibility of HA–CNT surface without any doubt.

• Implantation in bone tissue and for longer period (6 months, one year and more) is required for absolute assessment of in-vivo biocompatibility to establish the application of HA–CNT in orthopedic implants.

• Quantifying adhesion of bone cells on differently processed HA–CNT surfaces is vital to understand their in-vivo performance.

Future research activities, addressing all the issues mentioned above, will determine the potential of HA–CNT composite as a material for orthopedic applications.

Acknowledgement

Authors acknowledge support from the research facility at Advanced Materials Engineering and Research Institute (AMERI) in Florida International University. A.A. acknowledges funding from the National Science Foundation CAREER Award (NSF-DMI-0547178). D.L. acknowledges support from Dissertation Year Fellowship by University
Fig. 37. (a) TEM observations of HA–CNT-coated titanium implants at 2200× magnification revealing perfectly restored bone and bone marrow with normal morphological feature; (b) modulus map from different regions in retrieved implant/coating/bone interfaces for HA–CNT, HA and Ti implant surfaces. The color scale for modulus maps is similar and varies between 0 and 250 GPa [180].