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Biomaterials for Total Joint Replacements

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Abstract	The role of the chemical-physical characteristics of the prosthetic biomaterials in the biomechanics of a total joint replacement is presented. The following main biomaterials are discussed: (1) the ultra high molecular weight polyethylene (UHMWPE): standard, cross linked, stabilized with vitamin E; (2) the polymethylmethacrylate (PMMA): standard cement, cements with low temperature polymerization, antibiotic-loaded cements; (3) the ceramic materials: oxide ceramics (over all Alumina-Zirconia Composites) as components of the artificial joint, and calcium phosphate ceramics as osteoconductive coatings on metal alloy components; (4) the metallic materials: stainless steel, alloys based on the Co-Cr system, Ti and its alloys. To know how the biomaterial modifies its mechanical properties in accordance with the manufacturing, sterilization, storage, handling, contact with- and reaction to the patient's tissues and fluids is fundamental for the researchers and the surgeons, allowing a successful implant.	
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Biomaterials for Total Joint Replacements

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The European Society for Biomaterials defines a *biomaterial* “a material that interacts with the biological systems to evaluate, treat, reinforce or replace a tissue, organ or function of the organism” and the *biocompatibility* “the ability of a material to perform with an appropriate host response in a specific application” [1]. Recently, a new concept of biocompatibility was suggested in relation with the new technologies [2] and the fourth generation of biomaterials, the so-called smart or biomimetic materials [3]. Biocompatibility of a biomaterials is tested by in vitro screening, in vivo testing and clinical monitoring; each step evaluates the biological response in different conditions. In vivo, few

seconds after the implantation, the biomaterial is rapidly adsorbed by proteins, whose quantity and organisation depend on the characteristics of the biomaterial, such as chemical composition of the bulk and surface, surface geometry, chemical and physical properties and the properties of the proteins. The host cells contact the protein layer: in total joint replacements, bone cells on growing on the prosthetic surface determine an *osseointegration*, fibrous cells as *fibrous fixation*. The production of wear and degradation particles, inevitable in all TJR, determines a biological response defined as *bioreactivity*; its major determinants are the particle size, concentration, surface chemical composition, surface energy, surface charge, surface roughness, particle shape and nature of adsorbed proteins; genetics might be influential in determining the biological response. The wear particles activate macrophages and initiate the inflammatory cascade resulting in bone loss and reduced bone production, prosthetic loosening and eventual TJR failure. New therapeutic strategies try to diminish particle-associated periprosthetic inflammation modifying the monocyte/macrophages migration and activation [4].

Some wear metal particles are able to accumulate in the periprosthetic tissues and enter in the bloodstream, and can be responsible for chromosomal aberrations and DNA damage, which may promote cancerogenesis. Genotoxicity or mutagenicity, and/or carcinogenicity were demonstrated in experimental studies with CoCr

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53 alloys, in accordance with epidemiological stud- 87
 54 ies concerning the association of exposure to 88
 55 chromate particles and the incidence of nasal and 89
 56 lung cancer. Nickel is demonstrated to be geno- 90
 57 toxic in vitro and carcinogenetic in vivo (lung and 91
 58 ethmoidal bone). However, after an average of 13 92
 59 years and up to 25 years of follow-up, no increased 93
 60 cancer risk in patients with conventional total hip 94
 61 replacements was demonstrated [5–7].

62 In some previously sensitised patients, abra- 95
 63 sion and corrosion products could behave like 96
 64 haptens, and the complex may stimulate memory- 97
 65 lymphocytes initiating an inflammatory process. In 98
 66 particular, metal particles can either act as haptens 99
 67 bindings to protein carriers, or as adjuvants, forming 100
 68 insoluble complexes with the antigens, initiating an 101
 69 immune response. Hypersensitivity reactions have 102
 70 been reported to be more frequent with stainless- 103
 71 steel or cobalt alloy than with titanium alloy; hyper- 104
 72 sensitivity to polymethylmethacrylate was found to 105
 73 be 50 % in failed total hip implants. 106

74 The probability of developing a metal allergy 107
 75 seems to be higher post-operatively and the risk 108
 76 further increased when failed implants were 109
 77 compared with stable TJRs [8]

the Ultra High Molecular Weight Polyethylene 87
 (UHMWPE) is used because of its biocompatibility 88
 and excellent mechanical properties. UHMWPE is 89
 a high density PE (HDPE) with molecular mass 90
 more than 2.000.000 amu; it is a semi-crystalline 91
 polymer with a set of ordered regions (crystal- 92
 line lamellae), where macromolecules are tightly 93
 packed and the density is at its highest, embedded 94
 in a disordered amorphous phase, where macro- 95
 molecules are randomly arranged and orientated. 96

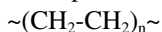
Table 5.1 shows the required characteristics of 97
 hopaedic UHMWPE according to ASTM F648- 98
 With an exception for the density (crystallinity 99
 degree is expressed as the percentage by weight of 100
 the crystalline regions present in the whole poly- 101
 mer), there are virtually no superior limits for the 102
 other characteristics. This means that UHMWPE 103
 can have different starting characteristics, whether 104
 chemical, physical or mechanical. It is worth men- 105
 tioning that the determination of these characteris- 106
 tics is carried out on the original material, before 107
 processing and sterilisation [9–11]. 108

Processing 109

The UHMWPE powder coming from the 110
 Ziegler-Natta polymerisation plant is processed 111
 by compression moulding and ram extrusion: 112
 both techniques use high pressure and controlled 113
 heating and cooling cycles, and do not signifi- 114
 cantly modify chemical, physical and structural 115
 characteristics of the starting polymer, with the 116
 exception of crystallinity (which is normally 117
 much higher in the pristine powder). Therefore 118
 all prosthetic components, ready to be sterilised, 119
 still retain all properties of the starting material. 120

Ultra High Molecular Weight Polyethylene (UHMWPE)

80 A macromolecular chain of polyethylene (PE) 110
 81 can be represented by the following formula: 111

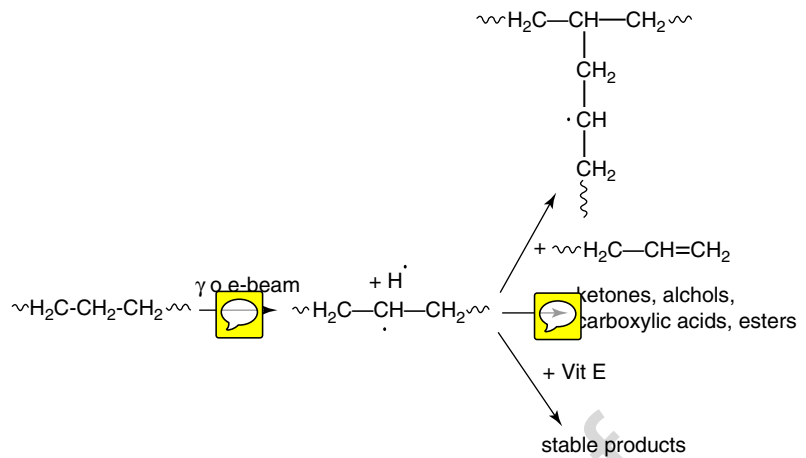


83 There are many types of PE, all characterised 113
 84 by the same structural unit, but with different 114
 85 lengths, different space arrangements and different 115
 86 chain imperfections. In total joint replacements, 116
 117
 118
 119
 120

t1.1 **Table 5.1** Requirements for UHMWPE fabricated forms, according to ASTM F 648

t1.2 Property (unit)	t1.3 Test method	Requirement for type I (GUR 1020)	Requirement for type II (GUR 1050)
t1.4 Density (g/cm ³)	ASTM D-792	0.927–0.944	0.927–0.944
t1.5 Ash (mg/kg) (maximum)		125	125
t1.6 Tensile strength (MPa)	ASTM D 638		
t1.7 Ultimate (minimum)		40	40
t1.8 Yield (minimum)		21	19
t1.9 Elongation (%)	ASTM D 638	380	340
t1.10 Izod impact strength (kJ/m ²) (min)	ASTM F 648–10 Annex A1	126	73
t1.11 Charpy impact strength (kJ/m ²) (min)	ISO/CD 11542/2.3	180	90

Fig. 5.1 The degradation of the UHMWPE induced by high energy radiation sterilization; in presence of oxygen, from the atmosphere, the process is called oxidation. Vitamin E is able to stabilize against oxidation



121 **Sterilisation**

122 The main sterilisation processes used nowadays
 123 employ ethylene oxide (EtO), gas-plasma (GP)
 124 and high-energy radiation (gamma radiation and
 125 electron beam) [9–11].

126 EtO and GP are surface sterilization meth-
 127 ods and do not significantly affect the physical,
 128 chemical and mechanical properties of prosthetic
 129 components. GP is based on the action of ionized
 130 gas (i.e. hydrogen peroxide or peracetic acid).

131 Gamma radiations are emitted during decay of
 132 a ^{60}Co unstable nucleus. The dose absorbed by
 133 prosthetic components is about 25–30 kGy and
 134 depends upon the geometry of the sample and its
 135 position in relation with the source.

136 Electron beam is produced by thermally excit-
 137 ing a tungsten filament; the emitted electrons are
 138 accelerated by electric fields up to 10 MeV and
 139 then conveyed onto the material to be sterilised.
 140 The advantages of this method are the easy control
 141 of the apparatus and the very short period of
 142 treatment (seconds).

143 **Degradation and Oxidation**

144 Gamma radiation and electron beam have a mean
 145 energy some orders of magnitude higher than that
 146 of polymeric chemical bonds and therefore gener-
 147 ate the scission of some chemical bonds of the
 148 UHMWPE and formation of free radicals. If even
 149 a single C-C bond of the UHMWPE chain is broken
 150 and $2^\circ \text{CH}_2\sim$ radicals are formed, the length

of the chain and consequently the molecular mass
 decrease, with worsening of some chemical and
 physical material characteristics. This process is
 called **degradation** and in presence of oxygen,
oxidation, which involves free radicals (Fig. 5.1).

The oxidative process depends on the radicals
 (formed during sterilisation) and on the amount
 of oxygen diffused into the PE components from
 the atmosphere during processing, sterilisation if
 conducted in presence of air and storage [12].

The distribution of oxidative products in the
 prosthetic component depends from the follow-
 ing variables: rate at which radiations is supplied,
 temperature of the sterilisation chamber, amount
 of oxygen present in the polymer when irradiated
 and diffused afterwards. Both in new and
 retrieved component, a *crown effect* or *white band*
 was the macroscopic evidence of this oxidation,
 responsible for many severe failures (delamina-
 tion and fracture) during service *in vivo* in years
 ‘90’. Unfortunately, the first dramatic failures of
 UHMWPE components in the mid 1980s were
 attributed to inadequate mechanical properties of
 the UHMWPE, despite the evidence that these
 properties were much better than those required
 by ASTM F648.

Packaging

An adequate packaging of the components is
 mandatory to assure the correct atmosphere in
 accordance with the chosen sterilization process;
 the packaging could be critical when high energy

182 radiation in vacuum or inert gases to reduce oxi-
183 dation is used. Currently employed packaging
184 can be included in three categories [13]:

- 185 – Gas-permeable packaging, adequate for EtO
186 and GP sterilization: a polyethylene tere-
187 phthalate (PET) blister with a Tyvek® cover;
- 188 – Polymer barrier packaging: multi-layer plastic
189 bags with gas-barrier properties with limited
190 but measurable permeability to oxygen;
- 191 – Aluminium barrier packaging: virtually
192 impermeable to gases.

193 Ultimately, a complete absence of oxidation is
194 obtained only by gas-sterilisation.

195 Debris and Diffusion

196 Polyethylene debris are particles loss due to fric-
197 tion, caused by the reciprocal movement of the
198 loaded articular surfaces: for equal mechanical
199 stress, material and interface, abrasion is func-
200 tion of time. Whereas dramatic failures due to
201 anomalous wear of heavily oxidised polyethyl-
202 ene have become quite uncommon nowadays,
203 the production of abraded particles remains a
204 problem in young patients whose life expectancy
205 and quality of life are very high. The debris initi-
206 ate an inflammatory reaction, the formation of a
207 loosening membrane and a secondary osteolysis.
208 The junctional tissue depends from number, size
209 and chemical structures of UHMWPE debris.
210 While pointing out that this topic is in continu-
211 ous development, it is important to realise that
212 the debris is not just simple UHMWPE particles,
213 but biologically active particles whose surface
214 interact with the human tissues according with
215 their macro and micromorphology, contact area,
216 molecules adsorpted on their surface, superficial
217 hydrophilic and hydrophobic character, release
218 of free radicals and time [9–11].

219 A process of adsorption and deep diffusion
220 into the UHMWPE prosthetic components of
221 organic molecules present in the synovial liquid,
222 such as cholesterol, ester of cholesterol, squalene,
223 β -carotene, takes place in vivo. This diffusion
224 explains the yellowish colour in some retrieved
225 components [14].

Crosslinked UHMWPE

226 To increase the abrasion resistance, crosslinked
227 UHMWPE (X-PE) appeared on the market in the
228 late 1990s [9–11, 15]. Crosslinking of a polymer
229 is the linking of two or more molecular chains
230 by means of chemical covalent bonds: macro
231 radical species, formed by treatment with high
232 energy, react with vinyl double bonds, linking the
233 polymer chains with a C-C stable chemical bond
234 and giving Y-crosslink. The X-PE can be repre-
235 sented as one long, branched molecule with infi-
236 nite molecular mass and consequent better wear
237 resistance properties than standard UHMWPE,
238 but also with some lower mechanical properties,
239 owing to chemical and physical modifications
240 induced by irradiation and heat treatment. 241

242 Commercially available X-PEs are obtained
243 by different crosslinking processes, mainly based
244 on gamma radiation or electron beam at doses
245 ranging from 60 to 100 kGy at room temperature
246 or in the molten state, depending on the manu-
247 facturer; the residual radicals are eliminated by
248 thermal treatment, sometime at temperature
249 below the melting point of the polymer (typically
250 at 130 °C) (annealing). The final sterilization is
251 obtained by EtO or gas-plasma or, in few cases,
252 by gamma radiation in low oxygen environment
253 [12].

254 Due to different crosslinking processes, the
255 commercial X-PEs can be very different with
256 variable properties, while standard UHMWPE
257 has and maintain its properties if processed and
258 sterilised in adequate ways.

259 Even if dramatic oxidation levels are not
260 observed in newly produced UHMWPE compo-
261 nents, it must be kept in mind that also very low
262 oxidation levels can lead to significant variations
263 in the mechanical properties of the polymer.

Vitamin E Stabilised UHMWPE

264 Vitamin E or, better, its synthetic derivative, alfa-
265 tocopherol, is employed to stabilize UHMWPE
266 against oxidation (ASTM F2695-12). As already
267 pointed out, PE is easily subject to oxidation,
268 which strongly compromises their mechani-
269 cal properties. The oxidation is basically due to
270

271 the reaction between macroradicals and oxygen
272 diffused into the polymer from the surround-
273 ing atmosphere; Vitamin E decreases the macro
274 alkyl radicals available to react with the oxygen
275 and thus to a significant slowdown of the oxi-
276 dative cascade [9–11, 15–17]. Unfortunately, a
277 decreased number of available alkyl radicals is
278 also responsible for a lower efficiency of cross-
279 linking at the same radiation dose, but a correct
280 vitamin E concentration and radiation dose deter-
281 mine an oxidatively stable UHMWPE, without
282 the need of a further thermal treatment, with
283 enough crosslink density and consequent resis-
284 tance to abrasion.

285 **Polymethylmethacrylate,** 286 **the Orthopaedic Cement**

287 Orthopaedic cement is basically poly(methyl
288 methacrylate) (PMMA) obtained by polymeris-
289 ing the methyl methacrylate monomer (MMA)
290 [18, 19]. Usually it is supplied in two separate
291 packages: a brown coloured vial (in order to
292 avoid any negative influence of the light on the
293 monomer) containing about 20 ml of transparent
294 liquid, and one package or two containing 40 g
295 of powder. The liquid contains: MMA, usually
296 N,N dimethyl-p-toluidine (DMPT) to accelerate
297 the polymerisation process in presence of radi-
298 cals, and traces of hydroquinone to avoid prema-
299 ture polymerisation of the monomer. The powder
300 is formed by pre-synthesised PMMA (at times
301 polymethylmethacrylate-styrene as copolymers
302 are used), dibenzoyl peroxide (DBP) and barium
303 sulphate (or zirconium dioxide), the latter may
304 be supplied in a separate package. PMMA is
305 in the shape of spherical particles having a vari-
306 able diameter between 30 and 250 μm ; the size
307 of the particles determines the viscosity of the
308 cement. When the contents of the two packages
309 are mixed, DBP initiates the radical process of
310 polymerisation through polymerisation accelera-
311 tor and the effect of polymerisation heat. Barium
312 sulphate makes the cement radio-opaque.

313 Cements produced by different industrial com-
314 panies have different chemical-physical charac-
315 teristics and mechanical properties due various
316 components and their relative concentrations.

Bone cement preparation is characterised by 317
three phases: the wetting phase corresponds to 318
mixing the solid part with the liquid, the setting 319
phase (divided into ‘dough time’ and ‘work- 320
ing time’) corresponds to the initial polymeri- 321
sation process (about 5 % of total), the curing 322
phase corresponds to the final hardening phase 323
and completion of the polymerisation process. 324
During mixing, benzoyl peroxide, present on 325
the surface of the PMMA powder, and DMPT 326
present in the liquid, interact and the polymeri- 327
sation process starts, mainly on the surface of 328
the pre-synthesised poly(methyl methacrylate). 329
Working time starts when a “dough” is obtained 330
which no longer sticks to gloves and tempera- 331
ture increase of the cement is minimal, corre- 332
sponding to minimal transformation of MMA to 333
PMMA. The final polymerisation phase is char- 334
acterised by the rapid increase of polymerisa- 335
tion rate and temperature. The time required for the 336
various phases depend mainly on the tempera- 337
ture in the operating theatre: a 10 $^{\circ}\text{C}$ increase 338
causes polymerisation to start twice as quickly, 339
cutting mixing times by half. After polymeriza- 340
tion, less than 5 % of MMA remains free and this 341
percentage may slowly spread into the body. The 342
MMA polymerization reaction is exothermic; the 343
high temperature favours DBP decomposition 344
leading to an increase in radical formation and 345
consequently an increase in polymerization pro- 346
cess. Therefore, polymerization speed is initially 347
minimal and gradually increases. Where process- 348
ing carried out in adiabatic conditions, the bone 349
cement temperature would reach 160 $^{\circ}\text{C}$. The 350
actual temperature reached by the cement dur- 351
ing the surgery depends on the balance between 352
quantity and speed with which the heat is pro- 353
duced, and how easily the heat is dispersed from 354
the surface into surrounding tissues. At the inter- 355
face with spongy bone, due to vascularisation 356
and the trabecular shape of the bone itself, tem- 357
peratures of 60 $^{\circ}\text{C}$ can be reached, while in the 358
centre of the mass of cement the temperature is 359
higher than 100 $^{\circ}\text{C}$. Schematically cement pro- 360
duces heat in function of the used amount, and 361
the temperature at the interface increases with the 362
higher quantity of cement. Based on this assump- 363
tion, an adequate surgical technique can lower 364
the temperature at the interface by using both 365

366 an adequate and not too thick layer of cement,
 367 and washing liquids in the final polymerization
 368 phase. Some cements are declared as “low tem-
 369 perature polymerization”. They are characterised
 370 by a lower ratio monomer MMA/polymer that
 371 proportionally lowers the heat developed during
 372 transformation of monomer into polymer. High
 373 temperature is sought when the cement is used
 374 as adjuvant in bone tumours to ensure “sterilisa-
 375 tion” of a bone surface from which the tumour
 376 has been removed; therefore in oncological sur-
 377 gery, standard PMMA is useful.

378 During polymerization reaction, a theoretical
 379 volumetric shrinking of the PMMA takes place
 380 proportional to the amount of MMA used; in the
 381 orthopaedic cement, the volumetric shrinking is
 382 7 % of the initial volume. Another characteristic
 383 of cement is the porosity due to CO₂ formed dur-
 384 ing decomposition of the initiator, MMA mono-
 385 mer evaporation, air-bubble formed during hand
 386 preparation of the mixture, and the expansion
 387 due to temperature increase during polymerisa-
 388 tion. In actual orthopaedic cements, the vacuum
 389 technique preparation decreases air-bubble for-
 390 mation; other factors cannot be eliminated.

391 Antibiotic-loaded cements are used in order to
 392 obtain a greater quantity of local antibiotic and
 393 to reduce the systemic quantity, thereby decreas-
 394 ing general toxicity; they are whether industrially
 395 packaged or prepared in the operating theatre
 396 according to the antibiogramme [20]. The state
 397 of the art on how the antibiotic manages to act
 398 is the following: the antibiotic, when soluble in
 399 water, dissolves from the surface of PMMA into
 400 the tissues; antibiotic molecules of notable size
 401 are physically blocked inside the bone cement
 402 and, therefore, cannot spread from inside the
 403 cement to the surface. The dissolution process
 404 depends on the type of antibiotic, on the charac-
 405 teristic of the surface of the cement and on the
 406 way the cement itself is prepared. When the anti-
 407 biotic is added to the cement during preparation
 408 of the cement itself, that is in the operating room,
 409 only a small part of the antibiotic molecules are
 410 casually on the surface of the cement and will be
 411 able to dissolve. This process explains why the
 412 actual antibiotic-loaded cements have a limited
 413 antiseptical action.

Ceramic Biomaterials 414

415 Ceramics are solid materials, which have as
 416 their essential component inorganic non-metallic
 417 materials. In joint replacements oxide ceramics
 418 are used as components of the artificial joint (ball
 419 heads and inserts in hip replacements, femo-
 420 ral component in knee replacements, glenoid in
 421 shoulder replacements), while calcium phosphate
 422 ceramics (CPCs) are used as osteoconductive
 423 coatings on metal alloy components.

Oxide Ceramics 424

425 Two ceramic oxides are used in joint replace-
 426 ments: alumina and zirconia. Both are ionic sol-
 427 ids, the high energy of the chemical bond giving
 428 them a high resistance to the corrosion, hardness,
 429 stiffness. The chemical stability of these oxides
 430 is the root of the excellent biological safety of
 431 their wear debris, a behaviour relevant for their
 432 intended use in arthroprostheses' bearings [21].
 433 So far (end 2014) more than 80 % of Total Hip
 434 Replacements (THR) in Italy, France, Germany
 435 and Austria are making use of ceramic ball
 436 heads, as well as in Japan and Korea, while in
 437 the USA ceramic ball heads are used in about
 438 20 % of THR only. The market leader CeramTec
 439 GmbH (Plochingen, Germany) declared to have
 440 sold by 2014 ten million of BIOLOX® ceramic
 441 bearing components. The behaviour of selected
 442 oxide ceramics is shown in Table 5.2.

Alumina 443

444 The development of alumina (aluminium oxide –
 445 Al₂O₃) as a biomaterial began in the mid-60s, the
 446 behaviour of alumina components (say total hip
 447 replacement – THR ball heads) were improved
 448 continuously over more than 40 years of clinical
 449 use, making alumina one of the better char-
 450 acterised biomaterials [22]. The material used in
 451 biomedical application is α -alumina, known as
 452 *corundum*, one of the most stable oxides, unaf-
 453 fected by corrosion (e.g. absence of ion release
 454 from bulk materials and from wear debris) in
 455 the most adverse conditions. The biocompat-
 456 ibility of alumina is a well-established property.

t2.1 **Table 5.2** Indicative values of selected properties of selected oxide bioceramics

t2.2	Properties (unit)	Unit	BIOLOX® <i>forte</i>	Prozyr®	BIOLOX® <i>delta</i>
t2.3	Usual name		Alumina	Zirconia Y-TZP	Alumina Matrix Composite (AMC)
t2.4					
t2.5	Chemical composition	wt %	>99.8 Alpha-Alumina	ZrO ₂ +5,1 % Y ₂ O ₃	Al ₂ O ₃ : 74 Y-TZP: 24 Other oxides: 2
t2.6					
t2.7					
t2.8	Density	g/cm ³	3.97	6.08	4.37
t2.9	Average grain size	µm	1.75	<0.5	0.56 (Al ₂ O ₃) 0.15 (Y-TZP)
t2.10					
t2.11	Bending strength	MPa	630	>1500	1390
t2.12	Fracture toughness	MPa m ^{1/2}	3.2	9	6.5
t2.13	Elastic modulus	GPa	407	200	358
t2.14	Hardness	HV	1975	1200	1760

457 Notwithstanding the improvements introduced
458 in the processing of alumina ceramics for clinical
459 applications, the weak point of this alumina
460 remains its low toughness that limits the flex-
461 ibility in design of alumina components. For this
462 reason, alumina components today are used in
463 about 15–20 % only of the ceramic implants, the
464 balance being alumina-zirconia composites (see
465 section on “[Alumina-Zirconia Composites](#)”).

466 Zirconia

467 Zirconia (zirconium dioxide – ZrO₂) ceramics
468 were developed and introduced in clinical use
469 in the late 80s to overcome the toughness limita-
470 tion of alumina. The early developments were
471 oriented towards Magnesia-Partially Stabilised
472 Zirconia (Mg-PSZ), in which the tetragonal
473 phase is present within large cubic grains
474 (Ø40 ÷ 50 µm) forming the matrix, a coarse struc-
475 ture that may negatively influence the wear prop-
476 erties of joints. Most of the developments were
477 focused on Ytria stabilised Tetragonal Zirconia
478 Polycrystal (YTZP), a ceramic constituted by
479 tetragonal grains some hundreds of nanometer in
480 size which has been a standard bearing material
481 in orthopaedics up to the year 2000. The struc-
482 tural applications of zirconia ceramics are based
483 on the constrained tetragonal-to-monoclinic
484 (t-m) phase transformation, which acts as a dissi-
485 pative mechanism for fracture energy. Briefly, the
486 phase transformation is associated to the expan-
487 sion of zirconia lattice (4 vol% in free grains)
488 and to its change in shape of the crystal cells that

489 have to overcome the constraint of the matrix
490 grains. The process takes place at the expenses of
491 the elastic energy field (tensile) associated to the
492 developing crack, that to advance has in addition
493 to win the compressive stress field due to grain
494 t-m transformation. At a macroscopic level, this
495 results in a toughened ceramic material, having
496 bending strength twice the one of alumina (900–
497 1100 MPa Vs. 500–600 MPa).

498 The t-m phase transformation that gives to
499 zirconia its interesting behaviour is also its main
500 drawback: zirconia is a metastable material, and
501 its clinical outcomes were contradictory [23].
502 The worldwide recall of the zirconia Prozyr®
503 ball heads made by Saint Gobain Advanced
504 Ceramics Desmarquest (Evreux, France) led to
505 the practical abandon of zirconia in arthroplasty,
506 where thus far it is still used in some niche prod-
507 ucts only. On the other hand, zirconia has found
508 recently a wide field of application as a bioma-
509 terial in dentistry, for the construction of dental
510 implants, and of the structure of crowns, bridges,
511 dentures by CAD-CAM processing of presinter-
512 ed blanks [21].

513 Zirconia is also used as a coating obtained
514 by in-situ oxidation of zirconium-2,5Nb alloy
515 (Oxinium®, Smith & Nephew, London, UK).
516 In spite of many claims of good wear proper-
517 ties following total knee replacement either total
518 hip replacement with OxZr femoral component,
519 doubts have been recently raised about this tech-
520 nology in terms of wear reduction both in terms
521 cost/benefits gains. Namely, due to its thickness

522 (5 μm) the surface zirconia scale can be easily
523 scratched by third bodies, leading to the increased
524 wear of the polyethylene counterface [24].

525 Alumina-Zirconia Composites

526 The abandon of zirconia opened a technological
527 gap in arthroplasty. Then, manufacturers focused
528 their attention of alumina zirconia composites,
529 especially on two classes of materials called
530 Zirconia-Toughened Alumina (ZTA) when alu-
531 mina is the main component and zirconia the bal-
532 ance, either Alumina-Toughened Zirconia (ATZ)
533 when the main component is zirconia.

534 The first material of this class used in clinics is
535 BIOLOX Δ (Ceramtec GmbH, Plochingen,
536 Germany), which is formed by a matrix of chro-
537 mia-doped alumina containing 17 vol% Y-TZP
538 and 1 vol% of strontium zirconate platelets. For
539 its peculiar microstructure, this material do not
540 belong to any of the formerly described classes,
541 and was identified as AMC: Alumina Matrix
542 Composite. The finely and homogenous distribu-
543 tion of Y-TZP both of the platelets is obtained by
544 nucleation within the alumina matrix during the
545 sintering cycle.

546 The high bending strength and toughness of
547 BIOLOX Δ in comparison with alumina
548 and Y-TZP is due to the constrained t-m trans-
549 formation of the zirconia grains: the transforma-
550 tion imply the compressive deformation of the
551 alumina matrix that has an elastic modulus (e.g.
552 stiffness) twice the Y-TZP one (407 GPa Vs.
553 200 GPa). This increase the energy dissipated in
554 the phase transformation. In addition, the plate-
555 lets in BIOLOX Δ having width/length ratio
556 1:10 perform as a fibres reinforcing the material
557 contributing to increase the material toughness.
558 By December 2014 more than four million ball
559 heads, inserts and condyles for knee replace-
560 ments made out BIOLOX Δ have been sold
561 worldwide, making this composite the standard
562 "ceramic" in arthroplasty.

563 Nitride Ceramics

564 While titanium nitride (TiN) is clinical since a
565 long while as a protective coating on metallic

component of joint replacement bearings, bulk 566
silicon nitride (Si_3N_4) has been tested for use in 567
THR cups coupled to metallic either ceramic ball 568
heads, but the future of this ceramic in arthro- 569
plasty remains still unclear [25]. 570

571 Complications with Ceramic Bearings

572 Due to the improvements introduced in manufac- 572
turing, fractures of ceramic composites is today 573
a very rare event. Arthroprostheses Registry data 574
show that revision for fracture of ceramic compo- 575
nent occurs with a frequency lower that the one 576
of stem/neck fractures, either of collapse of the 577
polyethylene inlays [26]. Fractures are typically 578
associated to severe trauma either to technical 579
errors in handling the ceramic components. Insert 580
fractures are especially due to intraoperative mis- 581
positioning while the orientation of the cup is 582
the reason of edge loading of the bearing compo- 583
nents. Recently much attention was devoted 584
to noises from THR bearings. Spectrum analysis 585
demonstrated that the acoustical vibrations are 586
depending on specific features of the implants. 587
This explains also the prevalence of the prob- 588
lem in some Countries and its absence in others, 589
likely due to the distribution of the devices [27]. 590

591 Calcium Phosphate Ceramics

592 Calcium phosphate ceramics (CPCs) are since a 592
long time used to give bone-bonding behaviour 593
to the surfaces of metallic joint replacements 594
(e.g. on THR stems) to enhance bony fixation. 595
CPC osteoconductive coatings are a well estab- 596
lished technology in joint replacements and long 597
term follow-ups confirm the results obtained 598
in early works [28]. CPC are a family of compo- 599
und with different in vivo behaviour depend- 600
ing on a number of parameters especially on 601
Ca/P ratio the most stable being Hydroxyapatite 602
 $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ [29]. 603

604 Osteoconductive CP coatings are made by 604
plasma spray. A critical aspect in this technol- 605
ogy is the Ca/P ratio of the starting powder and 606
its crystallinity. Powder experience a severe 607

608 heating/cooling thermal cycle during this pro- 653
609 cess. Formation of amorphous phases and of 654
610 resorbable calcium phosphate ceramic (CPC) 655
611 compounds, segregation of CaO and oxidation 656
612 reactions must be carefully controlled. Namely, 657
613 the rate of bone formation and the resorption 658
614 of coating and its mechanical stability (shear 659
615 strength, bond strength, fatigue life) are depend- 660
616 ing on a number of parameters, like e.g. pres- 661
617 ence of leachable phases, crystallinity, residual 662
618 porosity [30]. 663

619 **Metallic Materials for Joint** 620 **Prosthesis**

621 Metallic materials with industrial relevance for 670
622 joint prostheses belong to three main groups 671
623 [31–36]: (i) stainless steel; (ii) alloys based on 672
624 the Co-Cr system; (iii) Ti and its alloys. (i) The 673
625 austenitic AISI 316 stainless steel was the first 674
626 material used for orthopaedic implants. When it 675
627 is specified as AISI 316 L, the carbon content is 676
628 limited to 0.03 wt% for improving the corrosion 677
629 resistance of this material. (ii) Co-Cr based alloys 678
630 have been used for total joint prostheses since the 679
631 early 1900s and are originating from modifica- 680
632 tions of dentistry alloy Vitallium (Haynes Stellite 681
633 alloy N. 21). They combine good mechanical 682
634 properties with a high biocompatibility, due to 683
635 the presence of Cr, which forms spontaneously 684
636 a protective oxide layer. The carbon content in 685
637 the alloy must be carefully controlled, because 686
638 the formation of carbide phases may be detri- 687
639 mental for mechanical properties. (iii) Ti and 688
640 Ti-based alloys are widely used as biomaterials 689
641 for their high biocompatibility, mainly due to a 690
642 high corrosion resistance related to the forma- 691
643 tion of a passive oxide layer at the surface. Good 692
644 mechanical properties and low density constitute 693
645 an additional benefit for joint prostheses produc- 694
646 tion. Commercially pure (cP) Ti is used in differ- 695
647 ent grades, as a function of the oxygen content 696
648 as impurity. Common Ti-based alloys contain 697
649 aluminium (Al) and vanadium (V), the last often 698
650 substituted by Niobium (Nb) in order to increase 699
651 biocompatibility. The main components and 700
652 physical properties of most widely used metallic

biomaterials for joint prosthesis are collected in 653
Table 5.3. 654

The industrial production of metallic compo- 655
nents for joint prosthesis may be carried out 656
in different steps. As a first step, raw metals and 657
alloys are processed into stock shapes, such as 658
bars, sheet, rods, plates, tubes, wires and pow- 659
ders. The second processing step is used to tai- 660
lor the microstructure of the alloy, which is 661
strongly related to the mechanical properties of 662
the implant, by means of thermo-mechanical 663
treatments. The transformation of stock materi- 664
als into final products may be obtained by invest- 665
ment casting, machining, forging, and sintering. 666
Techniques used to manufacture various alloys to 667
produce metallic biomaterials for joint prostheses 668
are collected in Table 5.4. Surface coatings aimed 669
to improve functional properties of implant (i.e. 670
biocompatibility, bone fixation) are often added 671
as a final step. Functionality and duration of 672
implants in a physiological environment are 673
very sensitive to surface properties, which may 674
be considered the most important and selective 675
aspect for joint prosthesis selection. Surface 676
treatments are mainly aimed to increase hard- 677
ness and strength of the surface layer, in order 678
to improve the resistance to wear and corrosion. 679

Even if metallic biomaterials show good static 680
mechanical properties, they may suffer signifi- 681
cantly for fatigue failures [37]. Fatigue strength 682
is defined as the highest periodic stress that does 683
not initiate a failure of the material after a given 684
number of cycles. For hip prostheses, an average 685
of $2 \cdot 10^6$ stress cycles per year can be estimated, 686
so that more than 10^8 cycles may be applied dur- 687
ing a lifetime. The applied stress for fatigue fail- 688
ures is in the elastic region of the static loading, 689
so that fatigue strength is significantly lower than 690
ultimate tensile strength. Metallic biomaterials 691
have fatigue strengths in air generally well above 692
the minimum required for joint prosthesis appli- 693
cations. Mechanical properties of most widely 694
used metallic biomaterials for joint prostheses 695
are collected in Table 5.3, together with those of 696
cortical bones for comparison. 697

Total joint replacements are subjected to 698
wear and abrasion so that the resistance against 699
them is an important criterion for biomaterials. 700

Table 5.3 Typical composition (maximum amount allowed, wt%), physical and mechanical properties of metallic biomaterials

Materials	Main comp.	Other comp. (max wt%)	Density (g cm ⁻³)	Yield strength (MPa)	Ultimate tensile strength (MPa)	Fatigue strength (10 ⁷ cycles) MPa	Fracture toughness (MPa m ^{1/2})	Elastic modulus (GPa)	Elongation at fracture (%)
Stainless steels AISI 316	Fe	Ni (14), Cr (19), Mo (2.5), Mn (2)	7.5–8.0	170–790	480–1000	180–550	75–85	190–200	10–50
Co-Cr based alloys	Co	Cr (30), Ni (37), Mo (10.5), Mn (2)	8.2–9.1	250–1500	650–1800	300–950	50–60	210–240	8–50
cP-Ti	Ti	Fe (0.5), O (0.4)	4.5	170–485	240–550	200–330	65–75	110	15–25
Ti based alloys	Ti	Al (6.5), V (4.5), Nb (7.5), Fe (3), Mo (15), Zr (6)	4.4–5.3	800–1050	900–1100	450–650	50–55	75–115	8–20
Cortical bone					80–150	30	2–12	14–22	0–2

t3.1

t3.2

t3.3

t3.4

t3.5

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t3.18

t4.1 **Table 5.4** Techniques used to produce metallic biomaterials for total joint replacements

t4.2	Technique	Stainless steels	Co-Cr based alloys	cP-Ti	Ti based alloys
t4.3	Casting	Not used	Investment casting	Difficult	Difficult
t4.4	Machining	Possible	Difficult	Possible	Possible
t4.5	Cold working	Rolling	Difficult	Rolling	Difficult
t4.6	Hot working	Wrought, forged	Wrought, forged	Not used	Wrought, forged
t4.7	Sintering	Possible	Hot isostatic pressing	Not used	Not used
t4.8	Thermal treatments	Recrystallisation	Precipitation hardening	Recrystallisation	Precipitation hardening

701 High carbon Co-Cr based alloys (F75) improve
 702 significantly mechanical properties after work-
 703 ing, so that small plastic deformations at the
 704 surface significantly increase the hardness of the
 705 alloy and, as a consequence, its wear resistance.
 706 In addition, the presence of fine dispersed hard
 707 carbides increases the wear resistance of these
 708 alloys. Oxide films formed by passivation at
 709 the surface of the Cr and Ti containing alloys
 710 are generally resistant to abrasion [38]. Load
 711 required to fracture the oxide surface film is
 712 lower for Ti-based alloys with respect to Co-Cr
 713 based alloy.

714 In conclusion, the ideal alloy should have the
 715 elastic modulus of bone, the strength of cobalt-
 716 chromium alloys, the corrosion resistance and
 717 biocompatibility of titanium alloys, and the fab-
 718 rication cost of stainless steels [35, 36]. Each
 719 material has advantages and disadvantages,
 720 which drive applications. Stainless steels have
 721 good corrosion and fatigue resistance in short-
 722 term applications, have a low cost and they are
 723 easy to be machined, but tend to be corroded in
 724 long-term applications, have a high elastic mod-
 725 ulus and can produce Ni and Cr allergy. Co-Cr
 726 based alloys show long-term corrosion resis-
 727 tance, a high fatigue and wear resistance and a
 728 good biocompatibility, but they are difficult to
 729 machine, and thus expensive to process, and, like
 730 stainless steel, they suffer for a high elastic mod-
 731 ulus and Ni and Cr allergy. Ti-based alloys have
 732 a low density, joined with a relatively low elastic
 733 modulus, show the greatest corrosion resistance
 734 and have an excellent biocompatibility, but they
 735 have a relatively low shear strength and wear
 736 resistance and are quite expensive. As far as con-
 737 cern the total hip replacement, Table 5.5 reports
 738 the types of bearing types implanted in Italy on
 739 2014 [39].

Table 5.5 Types of total hip replacement bearings implanted in Italy on 2014

Bearing type		Share (%)	
Head	Cup		
Ceramic	Polyethylene	50.7	t5.3
Ceramic	Ceramic	28.5	t5.4
Metal	Polyethylene	16.7	t5.5
Metal	Metal	2.8	t5.6
Ceramic	Metal	0.7	t5.7
Metal	Ceramic	0.5	t5.8
Other		0.2	t5.9

Data from Torre et al. [39] t5.10
t5.11
t5.12

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