because of superior notch sensitivity and reverse-bending properties compared with Ti.

The density of Ti is about 57% of SS density. This decrease in density equates to a weight reduction of approximately 50% when comparing materials of similar volumes. The lower implant weight compared with an identical SS implant is not a major patient comfort factor for relatively small CMF implants. The modulus of elasticity for Ti is about 55% of SS, and for an equivalent cross-sectional area, the stiffness of a Ti implant is 55% of an SS implant. Physical properties are shown in **Table 1.4.1-2**.

The general corrosion and fretting corrosion properties of Ti and Ti alloy plates and screws are superior to SS. A reduction in the amount of in vivo corrosion products minimizes the foreign body reactions to maintain a satisfactory biocompatibility response. Titanium and Ti alloy implants may be mixed without causing any objectionable galvanic corrosion effects.

Implant quality SS and Ti materials are completely nonmagnetic and will not cause torque or displacement during magnetic resonance (MR) imaging. MR heating is a separate issue that is related to implant geometry. Long and thin implants, like K-wires, cables, and so on, with specific length-to-diameter ratios may show a temperature rise due to ½ wavelength resonance heating effects. ASTM F 2182 states that metal structures less than 2 cm in dimension are not expected to exhibit clinically significant radio frequency-induced temperature rise during MRI. Compared with SS, MR visualization of Ti is significantly improved because less artifact or starburst is created. Approximately 40% less MRI interference is experienced with Ti devices compared with SS devices due to the lower magnetic susceptibility of Ti, giving Ti implants a distinct advantage over SS in the CMF region. Turbo spin-echo and fast spin-echo MR pulse sequences tend to provide the lowest amount of artifact for all metal biomaterials.

Alloy	Density, gm/cc	Modulus of elasticity, GPa
All Ti grades	4.51	103
Ti-6Al-7Nb	4.52	105
(β) Ti-15Mo	4.96	78
(α + β) Ti-15Mo	4.96	105

Table 1.4.1-2 Physical properties of titanium (Ti) alloys.

2 Surfaces

Allergic reactions to nickel have been identified in about 3–5% of the general patient population and can approach 15% or higher in selected patient subsets. The 14.5% nickel content in SS is sufficient to cause nickel sensitivity reactions in patients who already have a history of metal allergies. Titanium does not contain nickel as an intentional addition and the typical nickel content is less than 0.02%. An advantage of Ti is its ability to readily form a naturally occurring oxide layer on its surface which provides additional corrosion protection. Therefore, when subjected to deformation damage during surgery, the oxide layer will spontaneously re-form as long as oxygen is present and will protect the material. This layer ranges between 5 and 6 nm in thickness but anodizing can increase this thickness. Final surface treatments for Ti implants include standard nitric acid immersion or electrochemical anodizing reactions that increase the thickness of the protective Ti oxide (TiO_2) or mixed oxide (ie, $TiO_2 + Al_20_3 + Nb_2O_5$) film. Titanium implants are immersed in a chemical solution and a known electrical voltage is applied for a specified time. The thickness of the oxide film determines the color that is observed due to visible light diffraction within the oxide film. No pigments or organic-coloring agents are present in the anodized Ti film. Titanium anodizing is capable of producing a variety of colors that permit the design of color-coded implant systems. Various studies indicate that anodizing removes objectionable surface contaminants, improves the corrosion resistance, has minimal effect on fatigue properties, and provides excellent biocompatibility. Multiple steam sterilization cycles will not significantly change the appearance of anodized Ti. Modified anodized films with unique properties and specialized organic coatings are under development to provide specific implant surface modifications. The anodized layer readily repassivates if the oxide becomes damaged, making Ti an extremely corrosion-resistant material. The oxide layer is capable of protecting cells from toxic-alloying elements and ultimately it is the oxide layer that produces a

cellular response and not that of the bulk material composite. Thermal and electrochemical anodization of Ti surfaces does not have any deleterious effect on fibroblast cell cytocompatibility *in vitro*. Moreover, there appears to be an absence of allergic reaction to Ti attributed to the absence of appreciable quantities of chromium, cobalt, and nickel, a distinct advantage over SS. Titanium dioxide is often used as a basis for many cosmetics because of the lack of allergic response experienced.

In 1997, Rogers et al showed that wear debris generated by Ti-6Al-4V incited an increase in inflammatory response factors, such as PGE2 and IL-1, in comparison with TAN (Ti-6% aluminum-7% niobium) and Ti. X-ray photoelectron spectrometry for surface chemical analysis reveals that an oxide film consisting of TiO_2, Al_2O_3, and NbO_5 occurs on the surface of TAN. The insolubility of this stable oxide layer is responsible for the excellent biopassivity reported, and the assorted oxide film demonstrated by TAN is chemically more stable compared with the oxide layer formed on Ti.

3 Tissue interactions

When inserting a wire, screw, pin, plate, or any other fracture fixation device into the body, regardless of the material or materials used, the implant is coated with a proteinaceous film within seconds of contact with the blood. Blood contains over 2,000 proteins which can interact with the surface of an implant. The proteins provide a provisional matrix for the cells to adhere to and represent the primary matrix in which cells interact. Platelets from the blood arrive at the scene from the blood and upon adherence to a surface the platelets contract, resulting in a process known as degranulation. This involves the release of intracellular contents, such as potent platelet activators, which in turn recruits additional platelets to the wound site. Macrophages and other inflammatory cells (granulocytes, lymphocytes, and monocytes) also infiltrate the hematoma and function to prevent infection and to secrete cytokines and growth factors. The growth factors possess chemotactic activity, thus serving as migratory signals for repair cells, such as osteoblasts, fibroblasts, monocytes, neutrophils, and leukocytes.

The cells arrive at the scene within minutes from the blood and can adhere to the protein matrix which has adsorbed to the surface (determined by the properties of that surface). However, the cells never interact directly with the bare implant surface (the oxide). Cells bind to Ti and its alloys through a series of adhesive molecules, such as vitronectin and fibronectin. Increased cell attachment is directly proportional to the amount of pre-adsorbed protein. Implant surface microtopography is important in osteoblast-mediated adhesion. Integrin-mediated binding to pre-adsorbed proteins on an implant is substrate dependent, eg, $\alpha 5\beta 1$, the receptor for fibronectin, increases on micro-rough Ti surfaces.

At the same time as the cell migration to the implant starts, the hematoma retracts. The ability of an implant surface to retain fibrin attachment during this retraction phase is crucial in determining if migrating cells will reach the device surface. The complexity of a micro-rough Ti surface oxide provides a 3-D topography so that fibrin remains sufficiently attached to the implant to withstand retraction, allowing for cell migration to the surface.

Cell adhesion is often followed later by either soft-tissue adhesion or eventual bony integration, depending on the implant surface and implantation site. The molecular events at the implant surface/tissue interface are controlled by the surface properties (the oxide, not by the underlying bulk material properties). The oxide surface properties include charge, chemistry, heterogeneity, hydrophobicity, and topography. Topography has the utmost significance for interaction with the surrounding tissues of currently used clinical metal implants. All the properties help determine which proteins adsorb to the surface, their orientation, and the types of intermolecular forces that occur between the surface and adsorbed proteins. These surface properties are not directly visible to the surgeon but are fundamental controllers of the biological success of an implant and all interrelate with each other, eg, changing surface chemistry alters the surface charge and can influence hydrophobicity and topography at the nano level (but the effects of the associated changes can be minimized).

Early soft-tissue integration with associated vascularization at the tissue-implant interface, without liquid-filled capsule