EPFL

Biomaterials for MX

MSE – 471

Prof. Maartje M.C. Bastings

Implants, foreign body reaction, case study

Course Content & Time Table

BLOCK 1: Introduction and materials overview

11-9	Lecture 1.	Intro to biomaterials and biology
18-9	Lecture 2.	Naturally derived biomaterials
25-9	**Lecture 3.**	**Implants and metals**
2-10	Lecture 4.	Polymers, Particles, and Surfaces

BLOCK 2: Interactions and specific applications

9-10	Lecture 5.	Materials for drug delivery and targeting
16-10	Lecture 6.	Materials for cell adhesion
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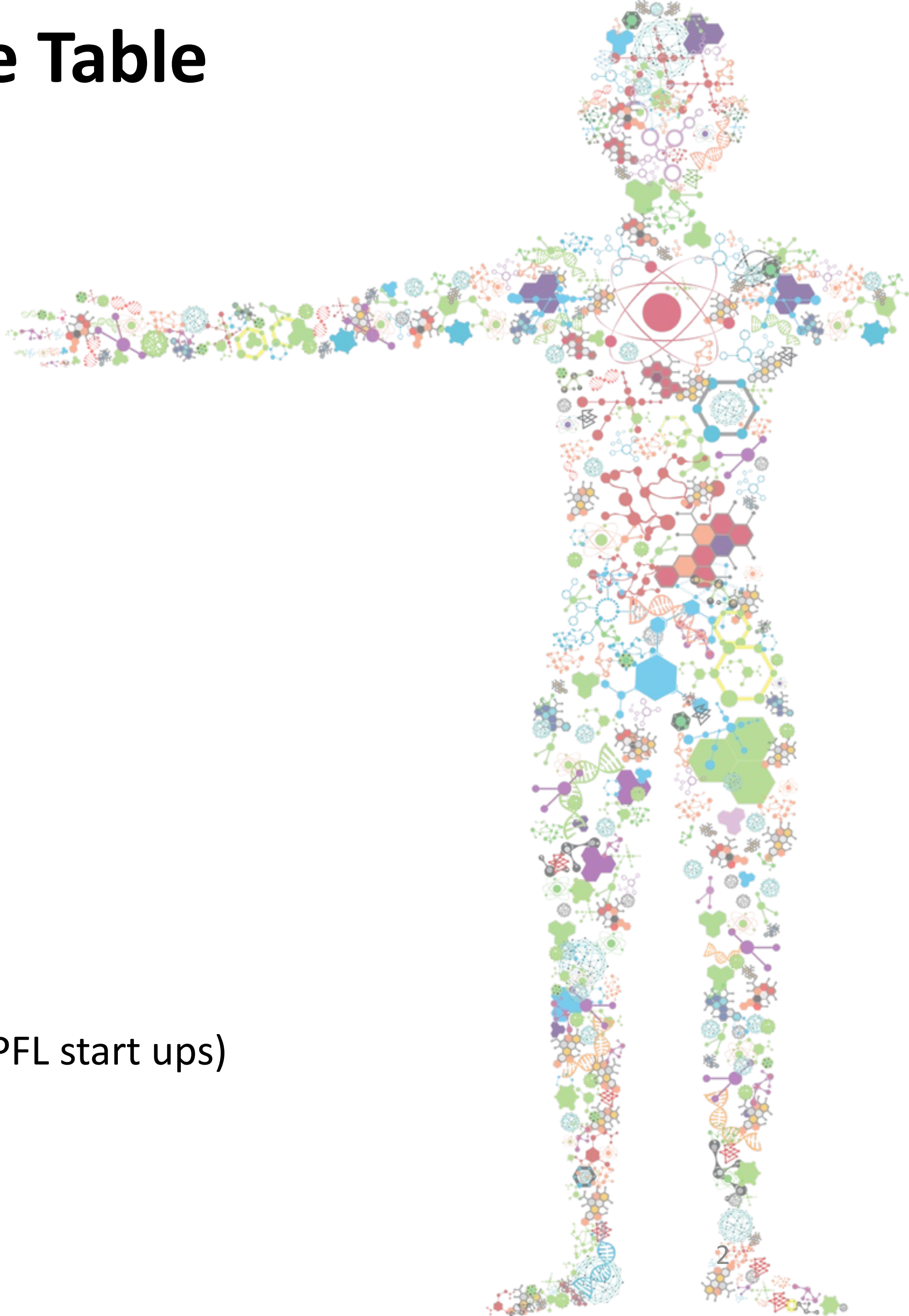
30-10	Lecture 7.	Materials for immune engineering
6-11	Lecture 8.	Materials for tissue engineering

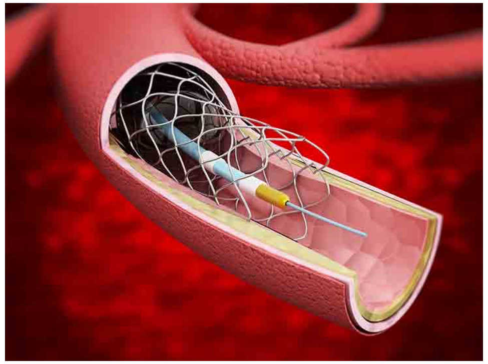
BLOCK 3: Measurements, regulation and translation

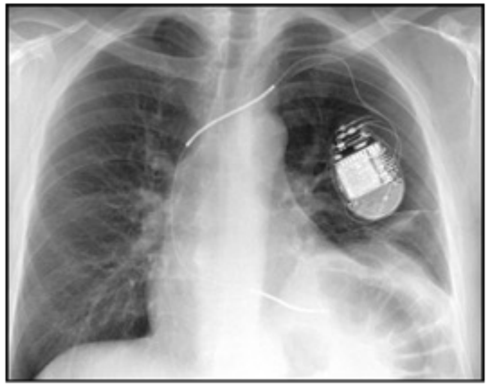
13-11	Lecture 9.	Characterization and performance
20-11	Lecture 10.	Sensors and diagnostic devices
27-11	Lecture 11.	Translation to industry, patents, spin-offs (EPFL start ups)
4-12	Lecture 12.	Regulatory aspects and trials (EPFL TTO)

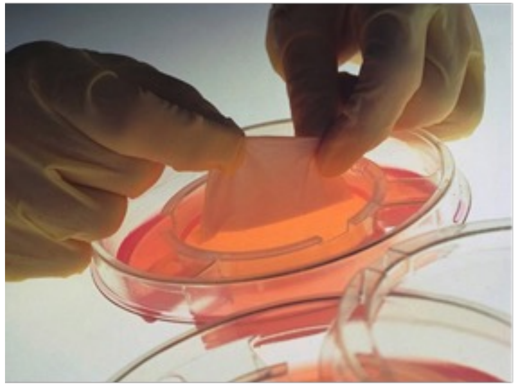
11-12	Lecture 13.	Revision and conclusion
18-12	Open discussion and hand in of lab papers	

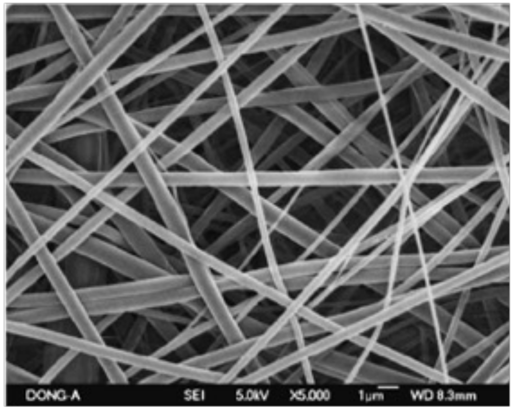


Manmade Materials



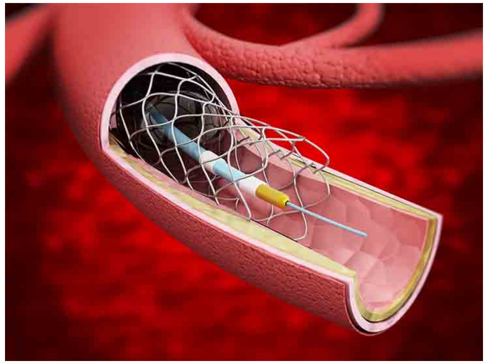


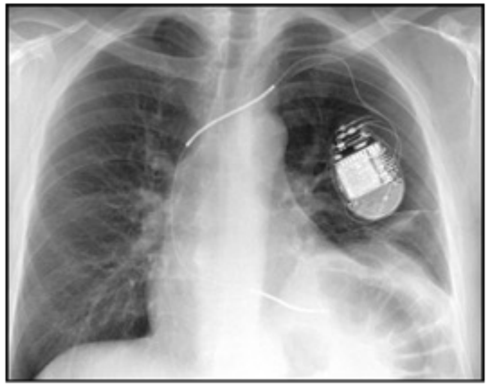


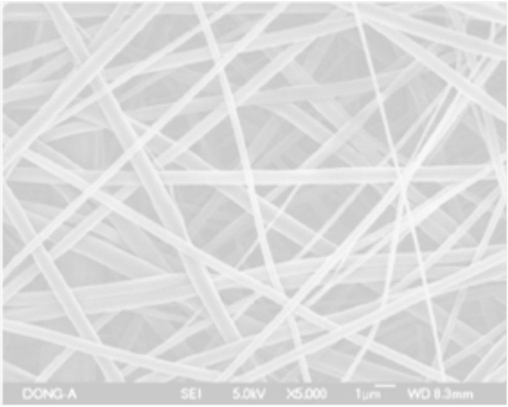


Manmade Materials





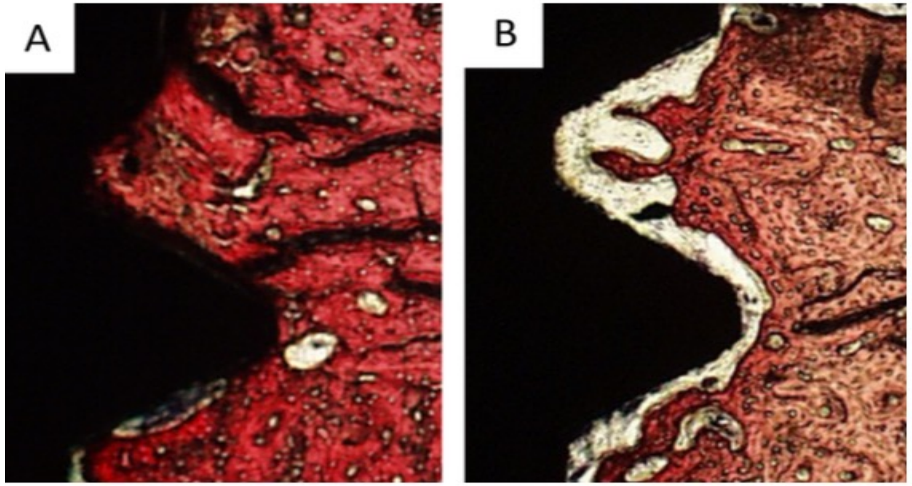


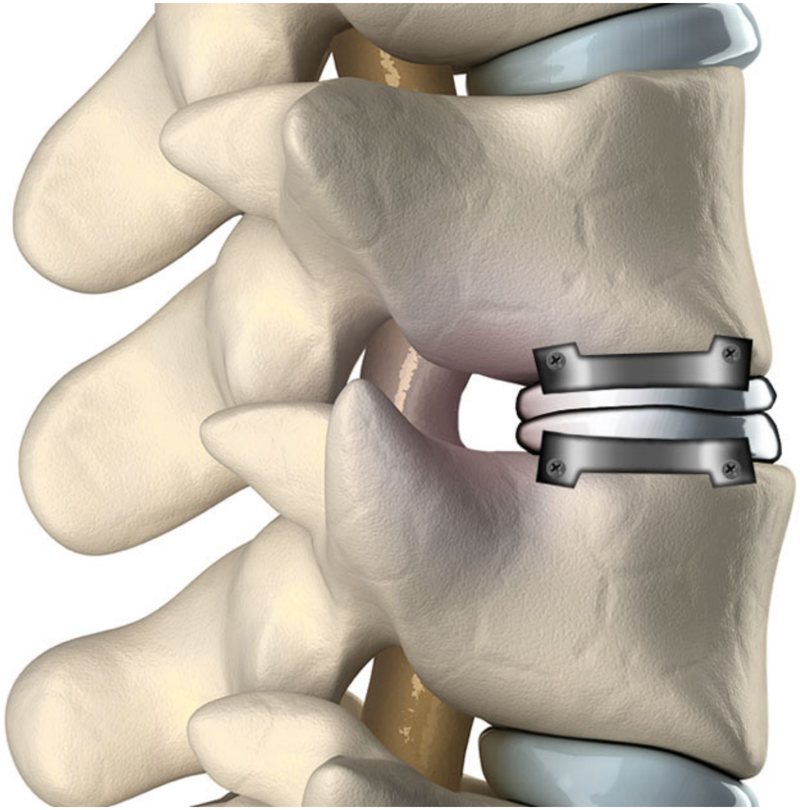

Today’s focus

Metals

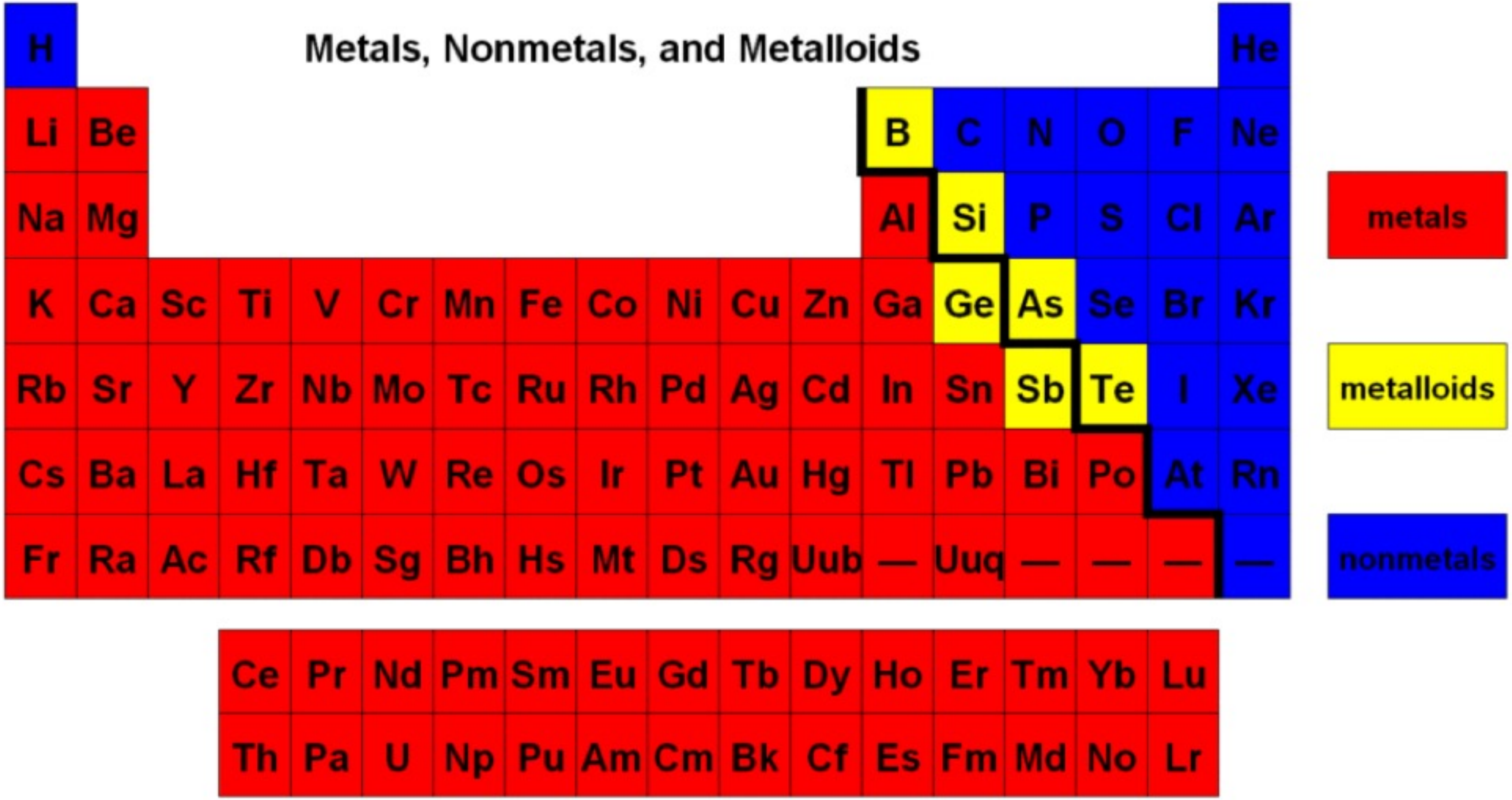
Osseo-integration
Foreign body response
Stress shielding



Case study: Spinal Implants



Most elements are Metals



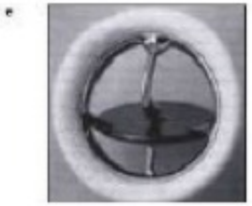
Metals

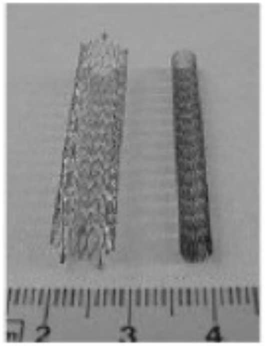
Metallic Biomaterials

Device	Annual # of Devices in USA
Intraocular Lenses (2003)	2,500,000
Vascular Grafts	300,000
Breast prostheses	250,000
**Heart Valves *(rings, cages)*	100,000 (some)
**Pacemakers	400,000
*Coronary Stents	1,500,000
*Hip Prostheses (2002)	250,000
*Knee Prostheses (2002)	250,000
*Dental Implants	910,000

Metal based (**Heart Valves through *Dental Implants)

- Source: Ratner, B.D. et al. "Biomaterials Science: An Introduction to Materials in Medicine, 2nd Edition, Elsevier Academic Press, San Diego, CA, 2004.
- In 2004 (unless otherwise stated)
- *indicates **all or predominantly metal**
- **indicates **metal-containing**




Why are Metals interesting Biomaterials?

Excellent mechanical properties for load bearing applications

- High fracture toughness
- High fatigue strength
- High yield strength
- Ductile

Can be fabricated into **various sizes and shapes**

Properties can be **altered** by physical processes (→ alloys)

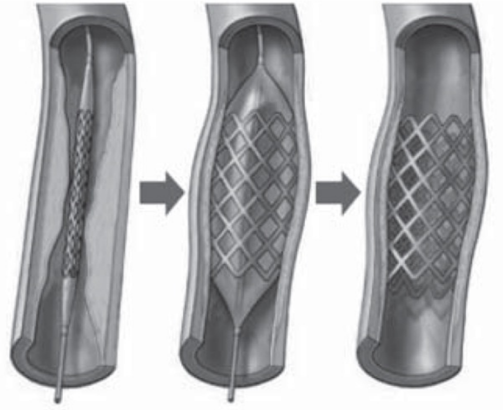
Good **resistance** to **external and internal environments**

- Easy to sterilize
- Stable microstructure at 37C

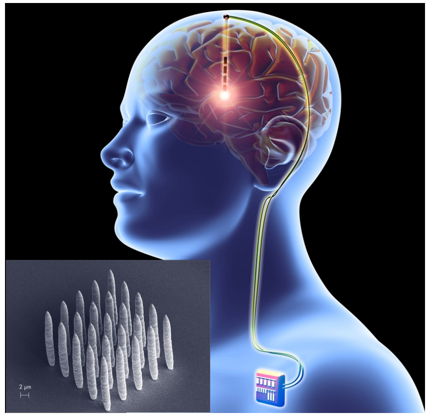
Orthopaedics

Dentistry

Cardiovascular



Neuroprostheses



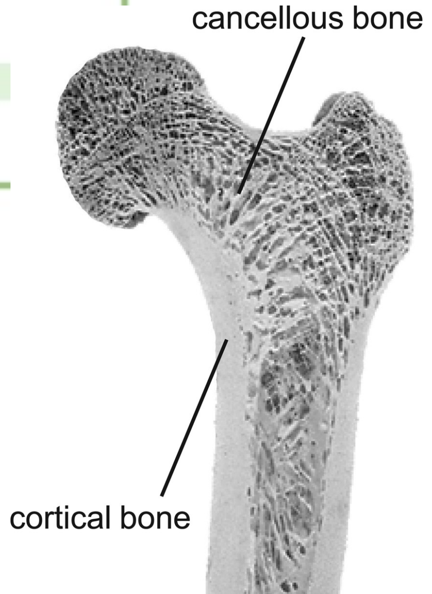
Surgical tools

Mechanical Properties

TABLE I.2.3.1 Typical Mechanical Properties of Implant Metals[a]

Material	ASTM Designation	Condition	Young's Modulus (GPa)	Yield Strength (MPa)	Tensile Strength (MPa)	Fatigue Endurance Limit Strength (at 10^7 cycles, $R = -1^c$) (MPa)
Stainless steel	F745	Annealed	190	221	483	221–280
	F55, F56, F138, F139	Annealed	190	331	586	241–276
		30% Cold-worked	190	792	930	310–448
		Cold forged	190	1213	1351	820
Co–Cr alloys	F75	As-cast/annealed	210	448–517	655–889	207–310
		P/M HIP[b]	253	841	1277	725–950
	F799	Hot forged	210	896–1200	1399–1586	600–896
	F90	Annealed	210	448–648	951–1220	Not available
		44% Cold-worked	210	1606	1896	586
	F562	Hot forged	232	965–1000	1206	500
		Cold-worked, aged	232	1500	1795	689–793 (axial tension $R = 0.05$, 30 Hz)
Ti alloys	F67	30% Cold-worked Grade 4	110	485	760	300
	F136	Forged annealed	116	896	965	620
		Forged, heat treated	116	1034	1103	620–689

Property	Cortical bone	Cancellous bone
Compressive strength (MPa)	100–230	2–12
Flexural, tensile strength (MPa)	50–150	10–20
Strain to failure (%)	1–3	5–7
Fracture toughness (MPam1/2)	2–12	–
Young's modulus (GPa)	7–30	0.5–0.05



Biocompatibility

Only a few metals / alloys are biocompatible

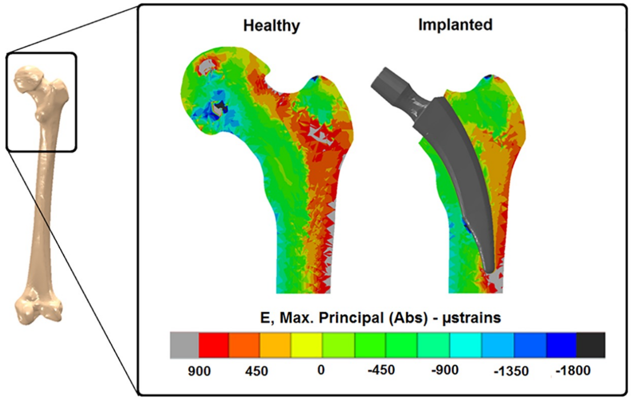
- Gold (dentistry)
- Platinum (electrodes)
- Stainless steel
- Co-Cr alloys
- Titanium and Ti-alloys (Ni-Ti)
- Magnesium alloys (bio corrodible)

Risks:

Nickel: cytotoxic and allergy
Titanium: inhibits osteoclast activity and reduces osteo-protein synthesis
Cobalt- chromium: formation of soft-tissue masses

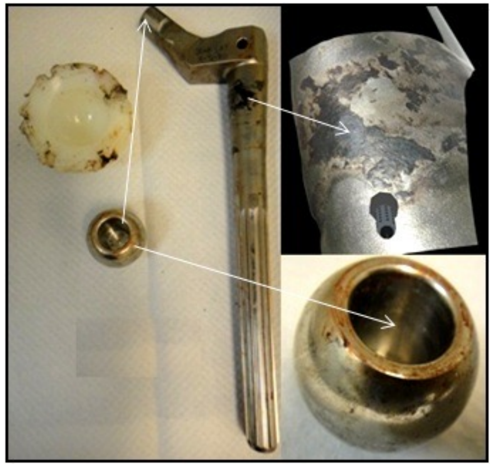
→ Need for coatings / alloys / surface architecture / …

Stress shielding

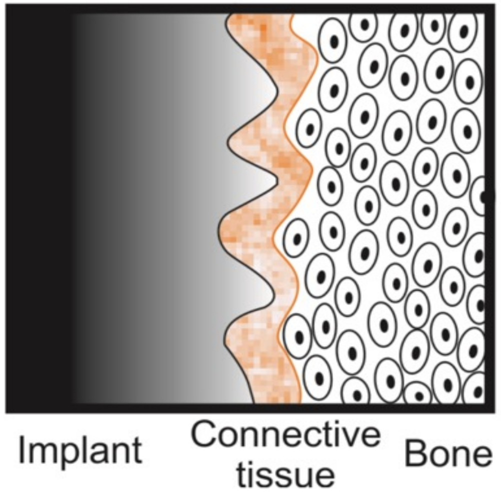


Corrosion

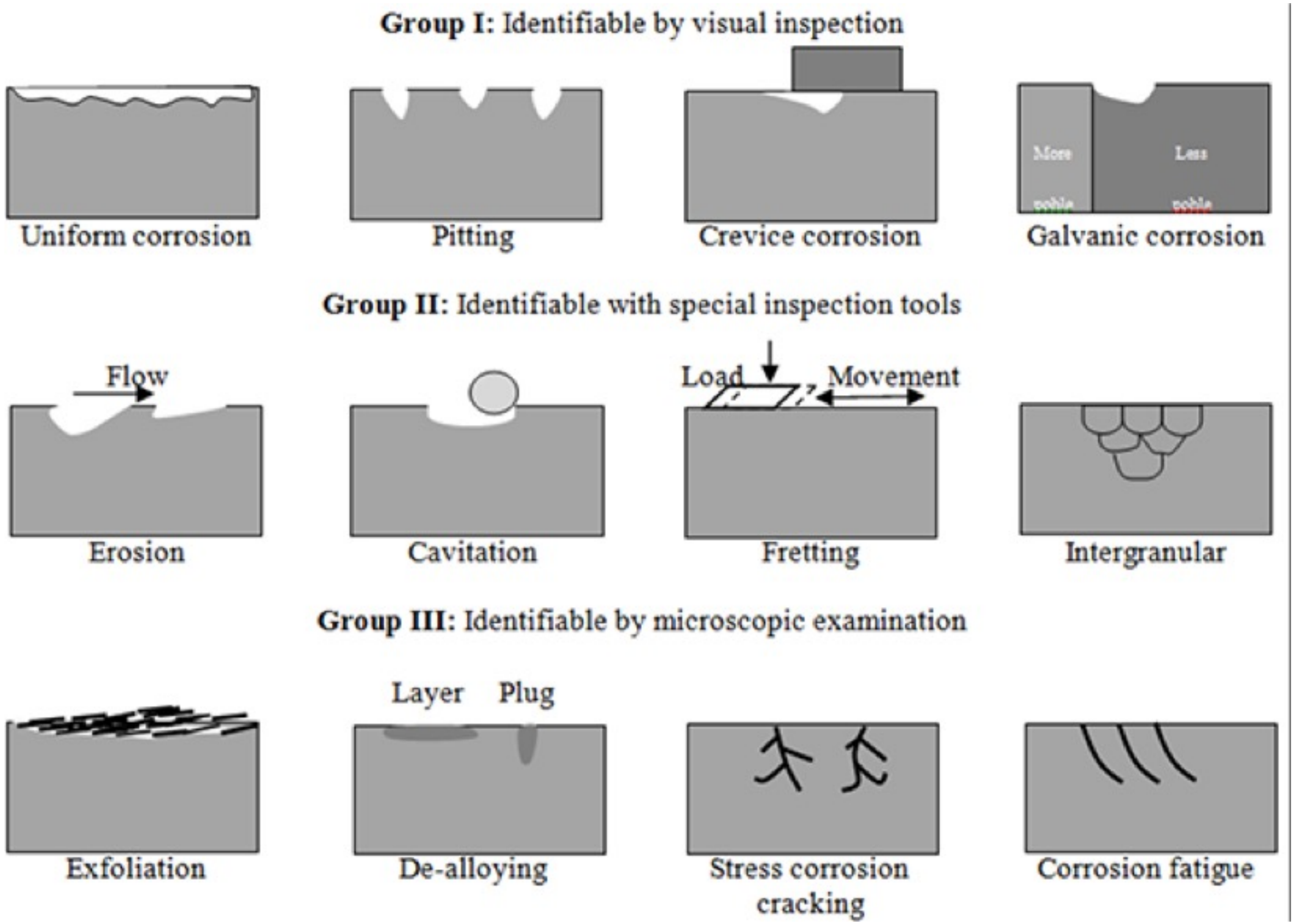
Toxicity/ Allergy



Osseo- integration

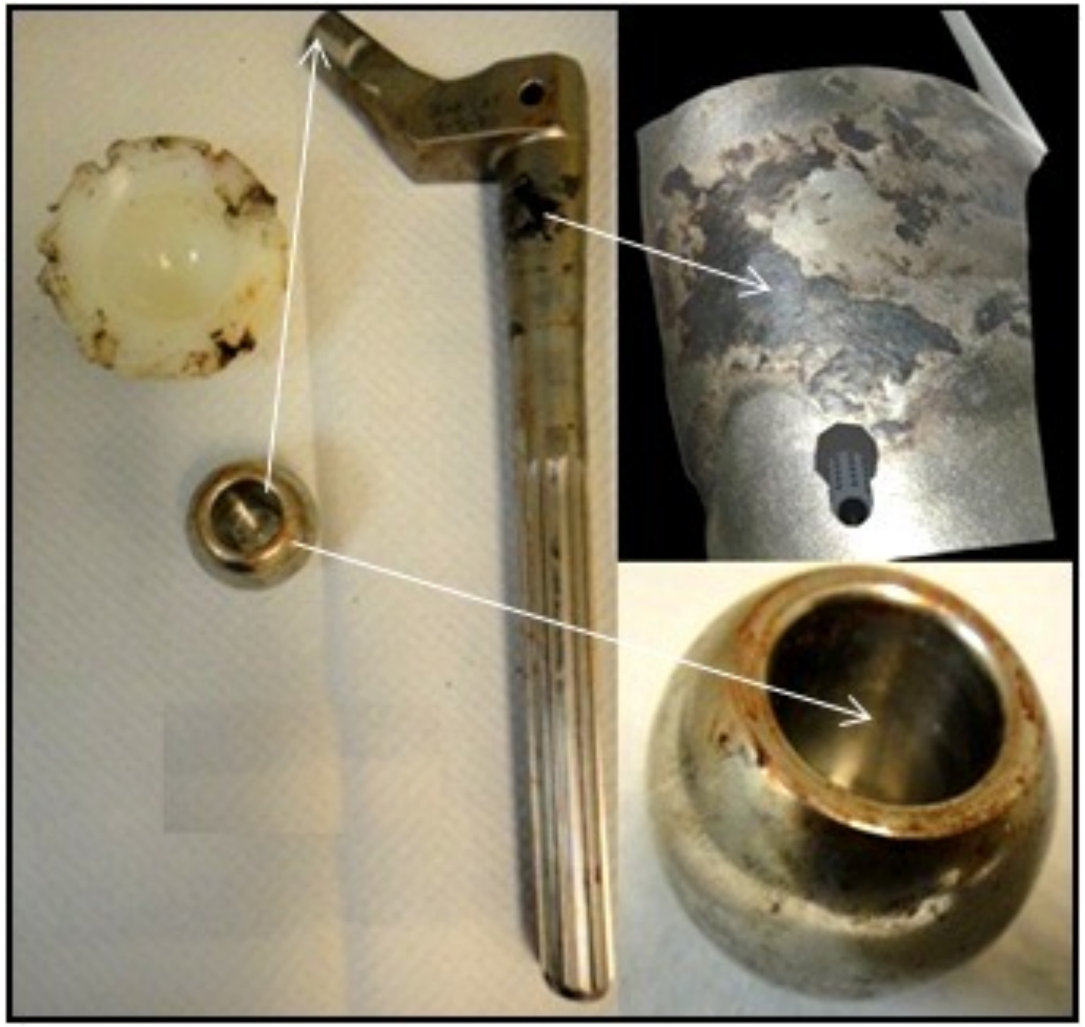


Challenges: Corrosion

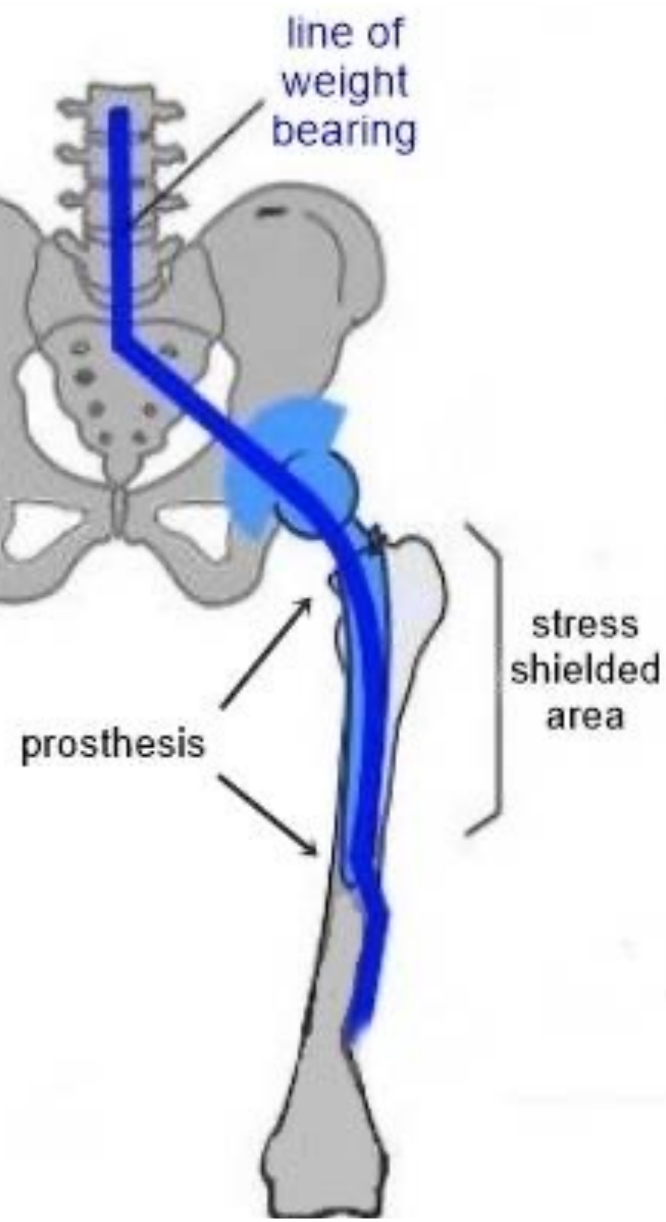


(2004) Different Forms of Corrosion Classified on the Basis of Appearence.
In: Bardal E. (eds) Corrosion and Protection. Engineering Materials and Processes. Springer, London

Corrosion on a hip implant



Stress Shielding



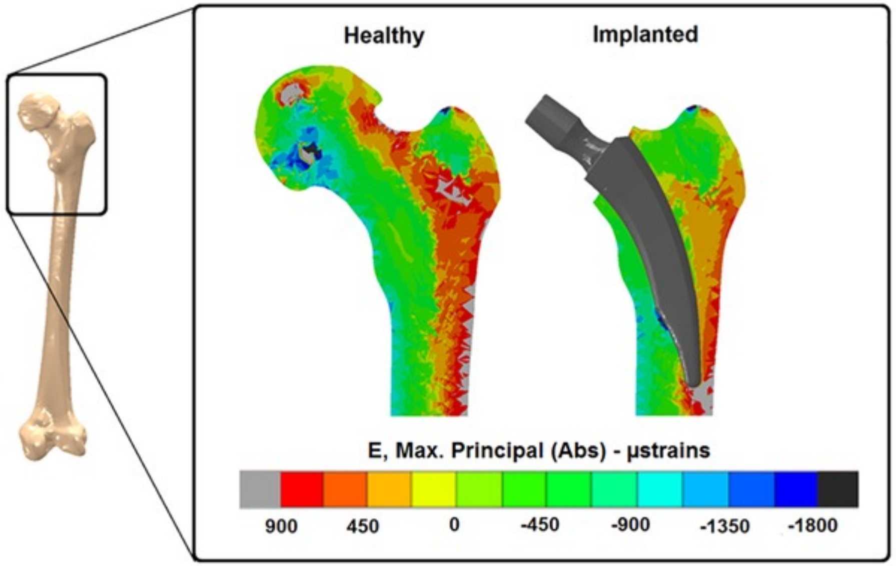
Loss in bone density as a result of **stress removal from the bone by implant**

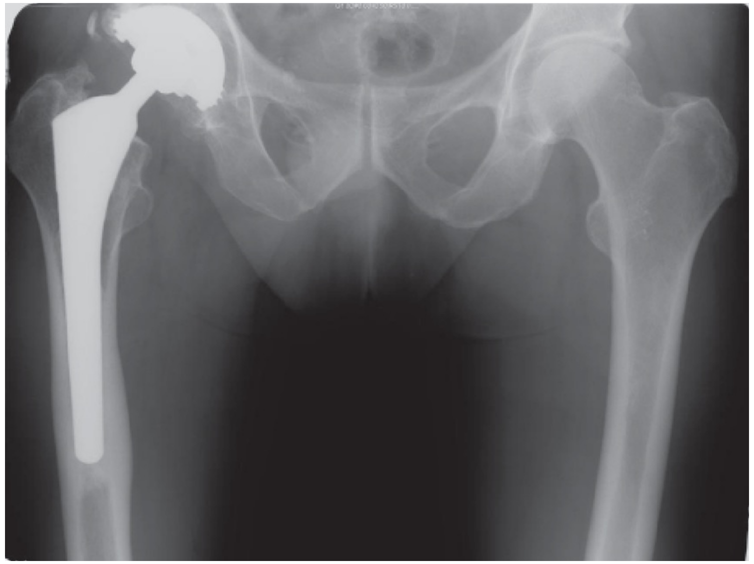
Bone in a healthy person will **remodel in response to the loads** it is placed under.

After implant is placed, the loading on a bone decreases, the bone will become less dense and weaker because there is **no stimulus for continued remodeling** that is required to maintain bone mass.

Result = implant loosening, failure (and no more bone)

Stiffness of material used should not be too high compared to bone.





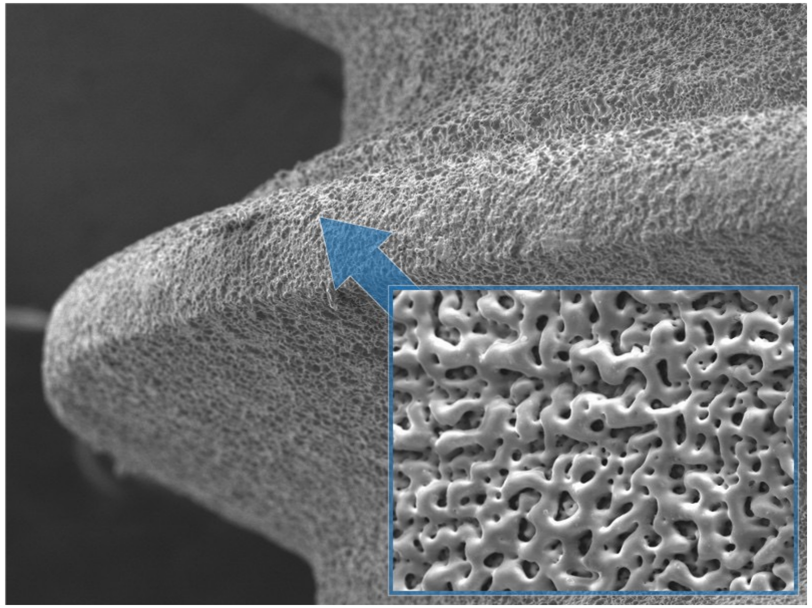
Osseointegration

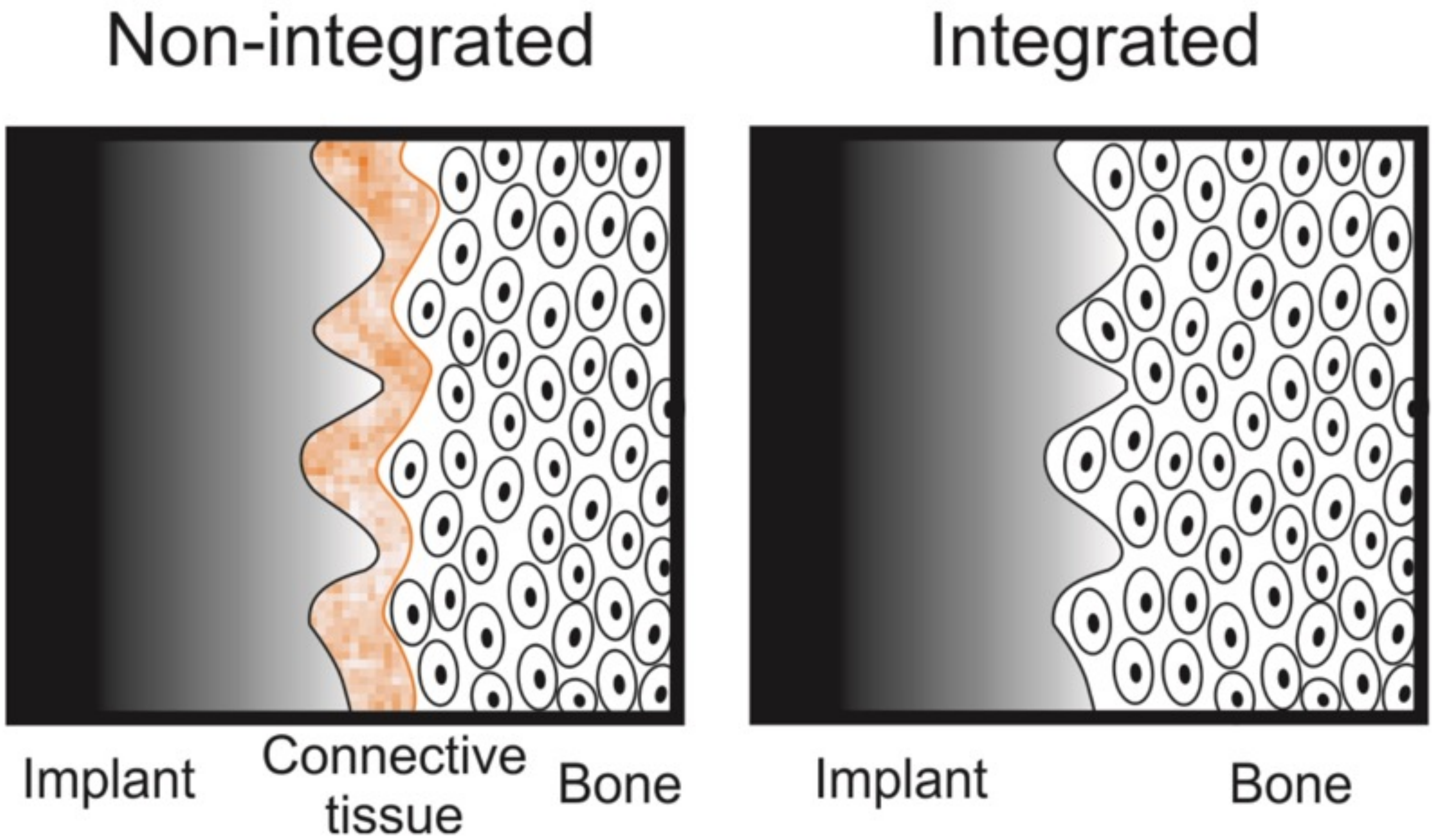
capacity for joining with bone and other tissue

- **First Step:** formation of a carbonated hydroxyapatite on surface via ion exchange
- **Second Step**: collagen fibers of host bone insert into the carbonated apatite layer

Engineering parameters:
Increasing the roughness
Surface treatments
Stimulate growth factor production

Risk: The inability of an implant surface to integrate with the adjacent bone and other tissues **results in implant loosening**

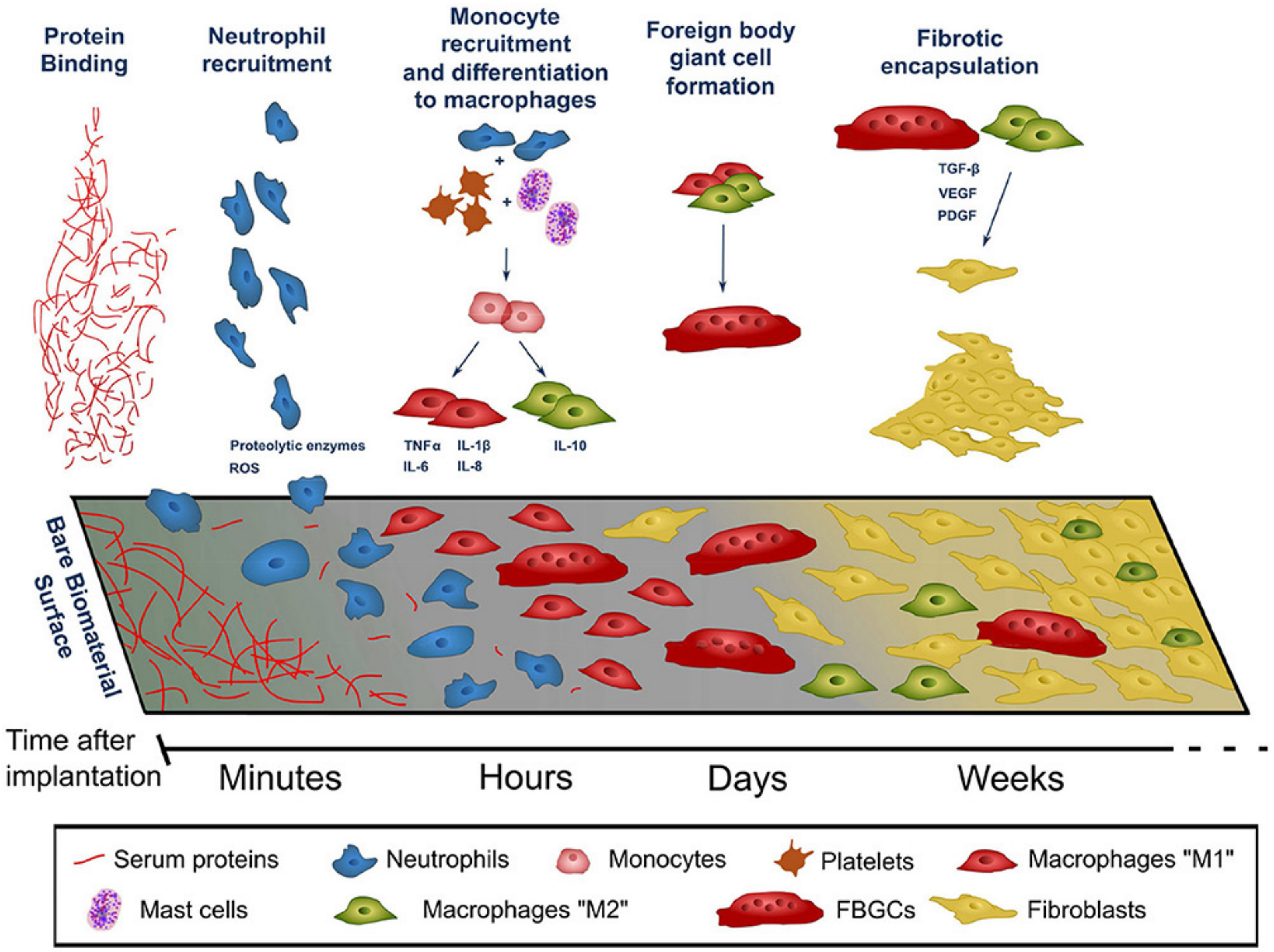




The foreign body response

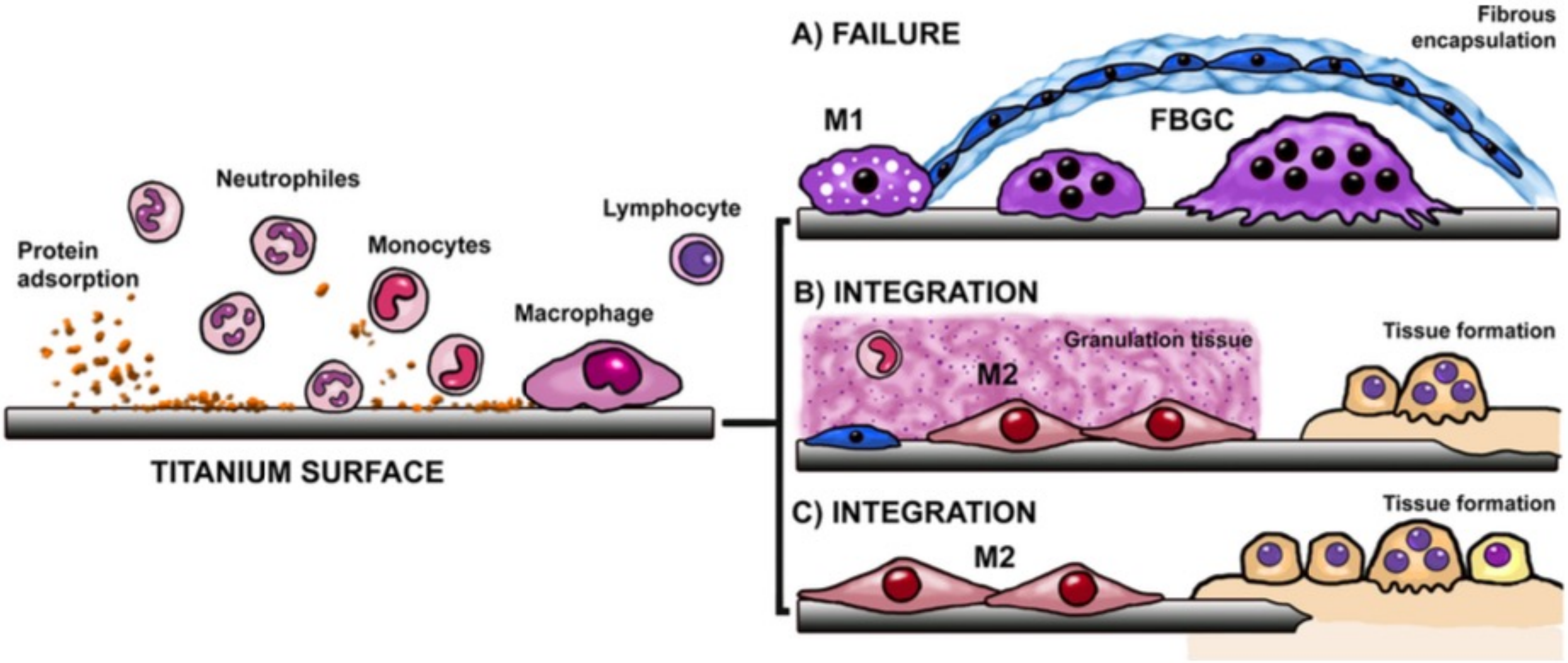
The composition of the cell population adhered to the surface of the implant **evolves over time** following the initial implantation.

Factors released by cells contribute to the recruitment of further cells and progression of FBR.



Front. Bioeng. Biotechnol., 2021
https://doi.org/10.3389/fbioe.2021.622524

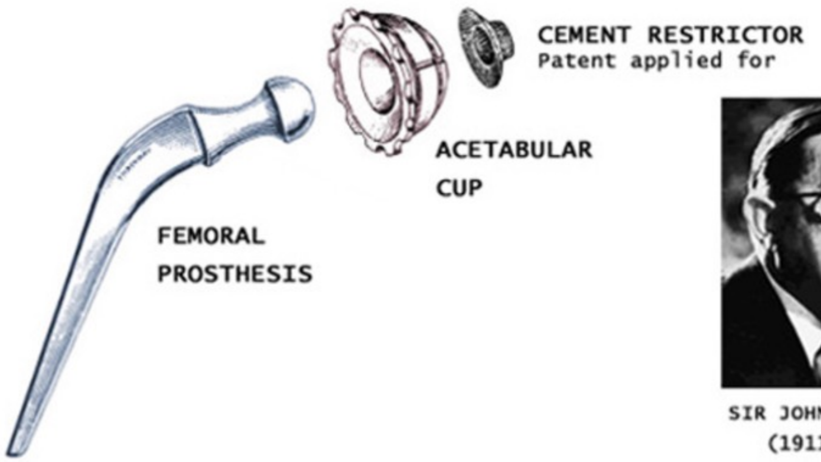
The foreign body response



DOI: 10.1021/acsbiomaterials.6b00604
ACS Biomater. Sci. Eng. 2017, 3, 1245−1261

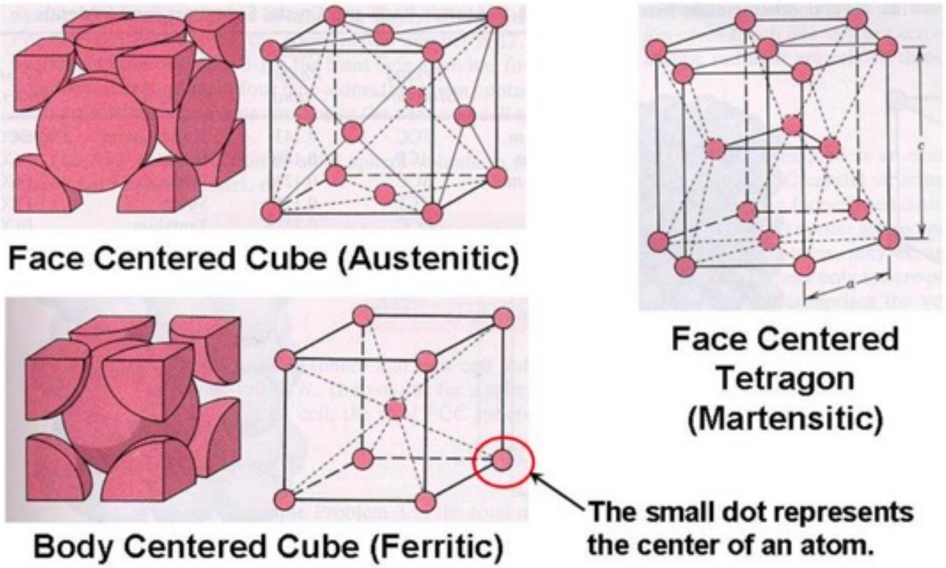
Stainless Steel

Stainless steels were the first metals to be used in orthopaedics in 1926.



SIR JOHN CHARNLEY (1911-1982)

Steel used in the hip implants until the end of 1970s



Non-magnetic!

Specially **AISI 316L is used in implants**
(316 = Mo-containing L = low carbon)

- **Ni** stabilises the **austenitic microstructure** of steel (note: allergic reactions)
- **Cr-containing steel** produces a thin and relatively **durable passivating oxide layer**
- **Mo** has a strong positive effect on pitting and crevice **corrosion resistance** in chloride-containing solutions

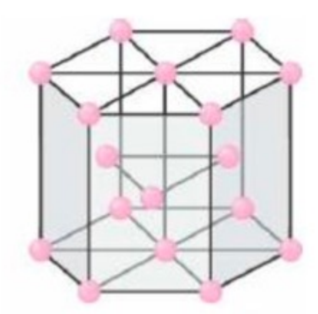
\+ Good corrosion and fatigue resistance in short-term applications
\+ Low cost
\+ Easy to be machined

\- Tend to be corroded in long-term applications
\- High modulus (stress shielding effect)
\- Ni and Cr allergy

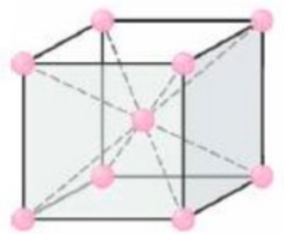
Typical applications:
Temporary implants such as fixation screws and plates

Titanium

Most flexible of metals used in orthopaedics
Light weight
Excellent corrosion resistance (Ca-P layer and surface oxide makes it inert)
Pure titanium can be used where strength is not required



HCP α-Ti

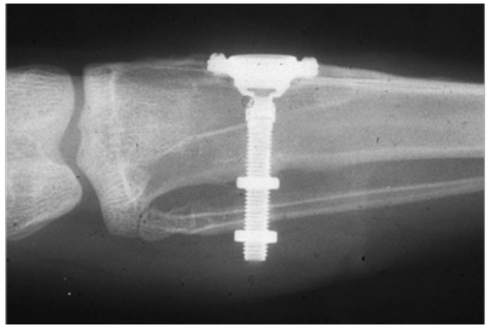


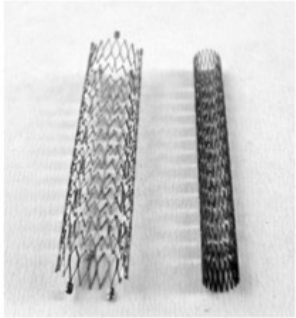
BCC β-Ti

α
- \+ corrosion resistance, biocompatibility
- \+ weldability
- \- poor forgeability, low strength

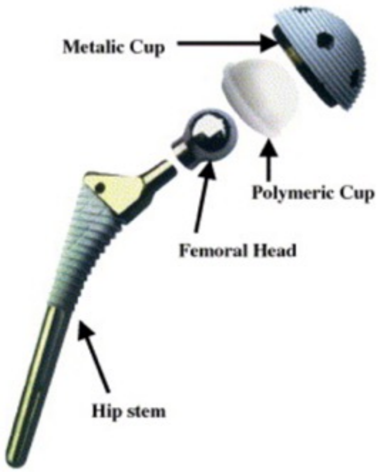
$\alpha - \beta$
- \+ can be strengthened by heat treatment

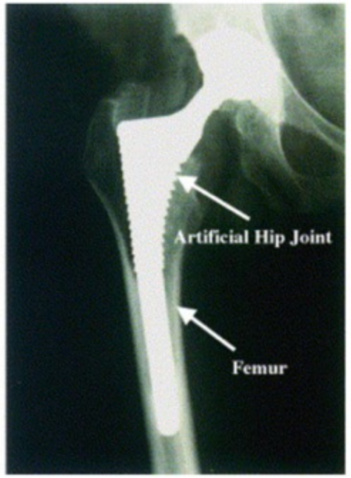
β
- \+ high hardenability
- \+ good ductility and toughness
- \- high density
- \- low creep strength
- \- low tensile ductility in the aged state
- \- low wear resistance

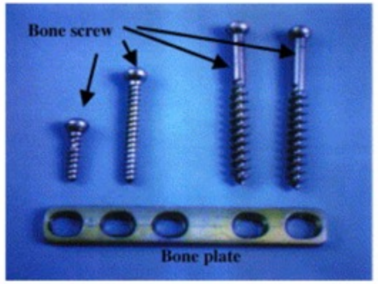


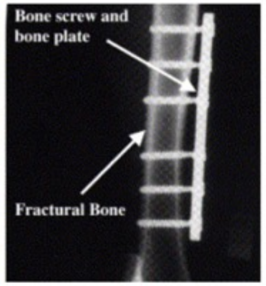


- since the 1970s



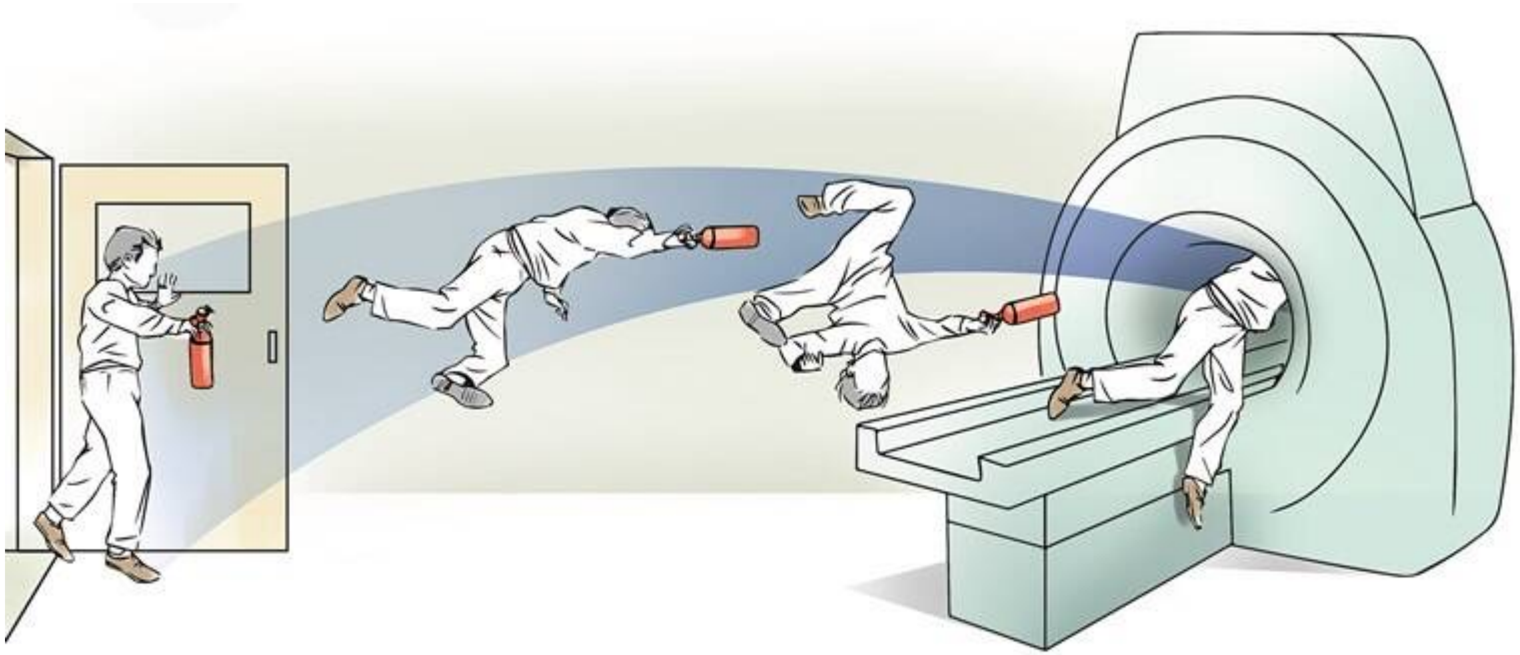




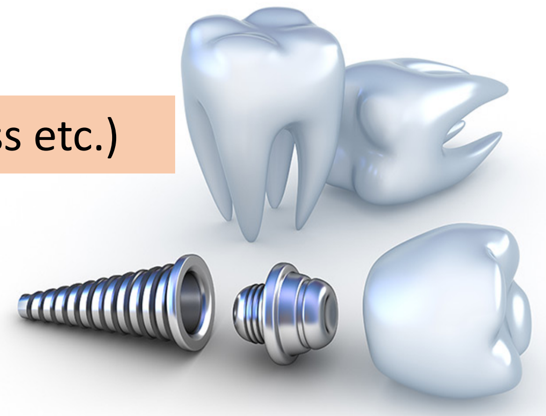


Magnetism

Class	Magnetic	Crystal Structure	Examples
Ferritic	Yes	BCC	405, 409, 430, 446
Austenitic	No	FCC	301, 304, 309, 316
Martensitic	Yes	BCT	403, 410, 416, 431
Duplex	Yes	Combination	329, 255c, 2205c
Precipitation Hardened	Yes	Combination	C450e, 15-5, 17-4



Alloys



Combine elements to obtained preferential properties (Corrosion, osseointegration, stiffness etc.)

- Stainless steel (AlSl316L) → non-magnetic
- Co-Cr alloys (Vitallium)
- Ti-alloys (Nitinol, Ti-6Al-4V))
- Magnesium alloys (bio corrodible)

Ti-6Al-4V (grade 5) alloy – (Titanium – Vanadium – Aluminium)
hard tissue replacement artificial bones, joints and dental implants.
low elastic modulus → smaller stress shielding.
surface modification to **improve osseointegration**.

Vitallium is an alloy of 65% cobalt, 30% chromium, 5% molybdenum.
Main use in dentistry and joints, due to **corrosion resistance**.

Nitinol (Ni-Ti 50-50): used in **orthodontics** for brackets and wires connecting the teeth. Following placement, temperature rises to ambient body temperature, nitinol wire contracts back to its original shape, applying a constant force to move the teeth. **No need to be retightened** as often as other wires because they can contract as the teeth move unlike conventional stainless steel wires.

The ideal metal for an implant is:

Biocompatible (non toxic, non carcinogenic, non immunogenic)

Strength (compressive, tensile, torsional)

Fatigue resistance

Resistance to corrosion and degradation

Osseo-integration (when applicable)

Imaging compatible (non-magnetic!!!)

Inexpensive

Implant Failure:

Brittle failure: screw head with poor ductility

Plastic failure: load > endurance limit (implant bends permanently)

Fatigue failure: cyclical (repetitive) loading

Poor osseointegration: loosening

Poor biocompatibility: Toxicity / allergy / immune reaction

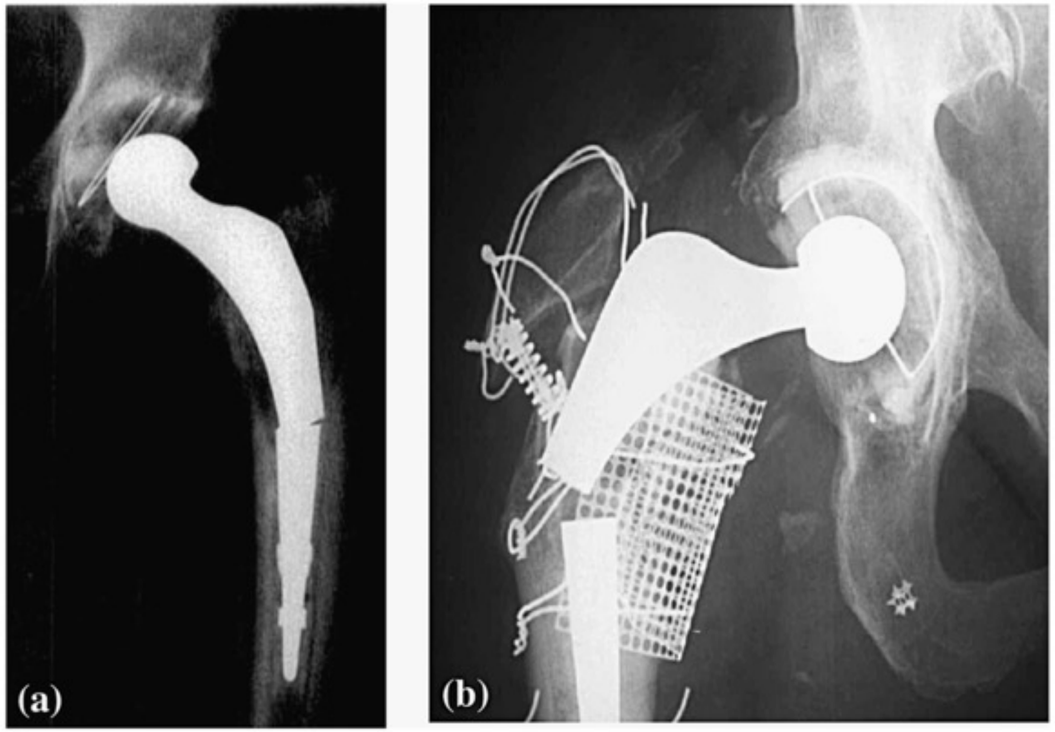
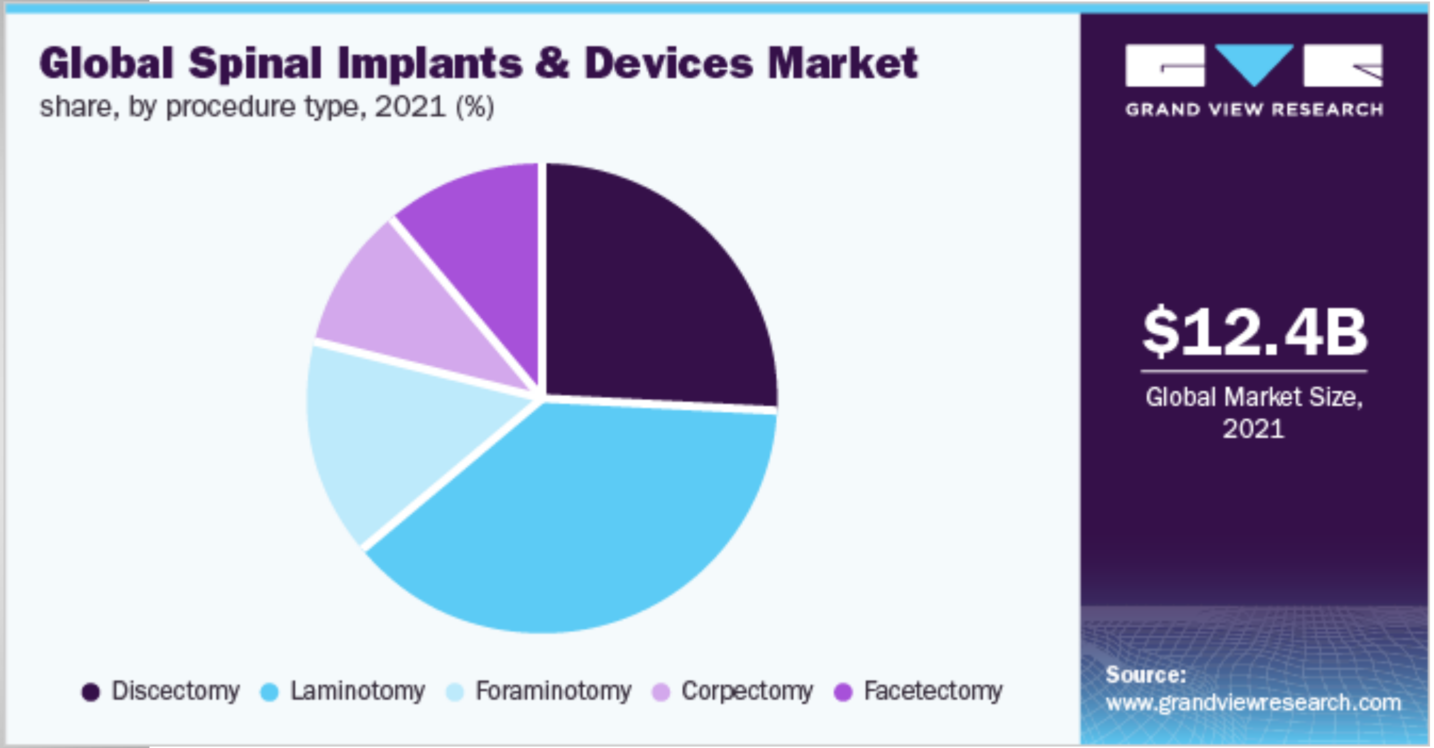


Fig. 11. (a) Stem fracture after 8.6 years. Endosteal bone lysis surrounds the proximal half of the stem. The stem has subsided 1.6 cm, partly within the cer
with the distal cement mantle. (b) Fractured Exeter stem after 3 years. Graft shows incorporation distal to the lesser trochanter and resorption prox

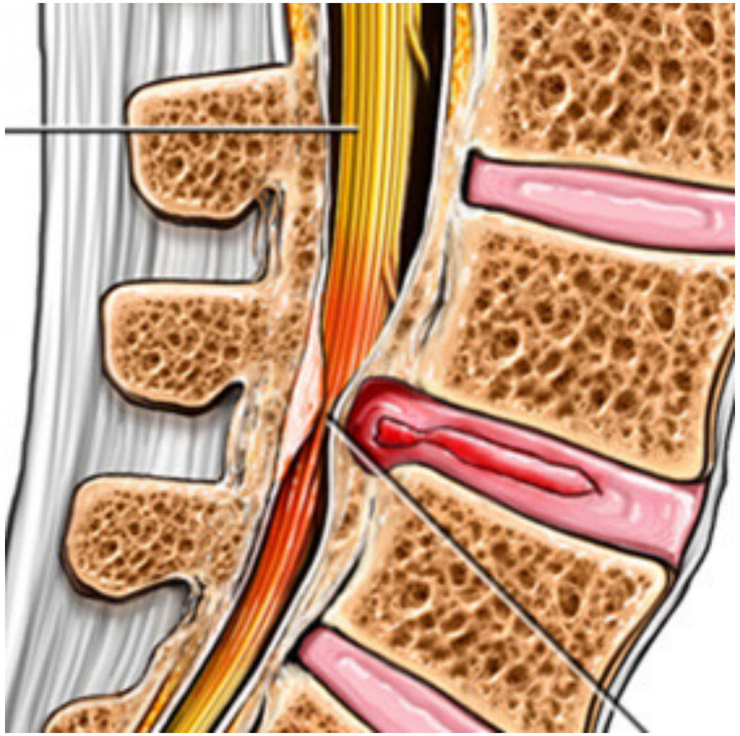
break

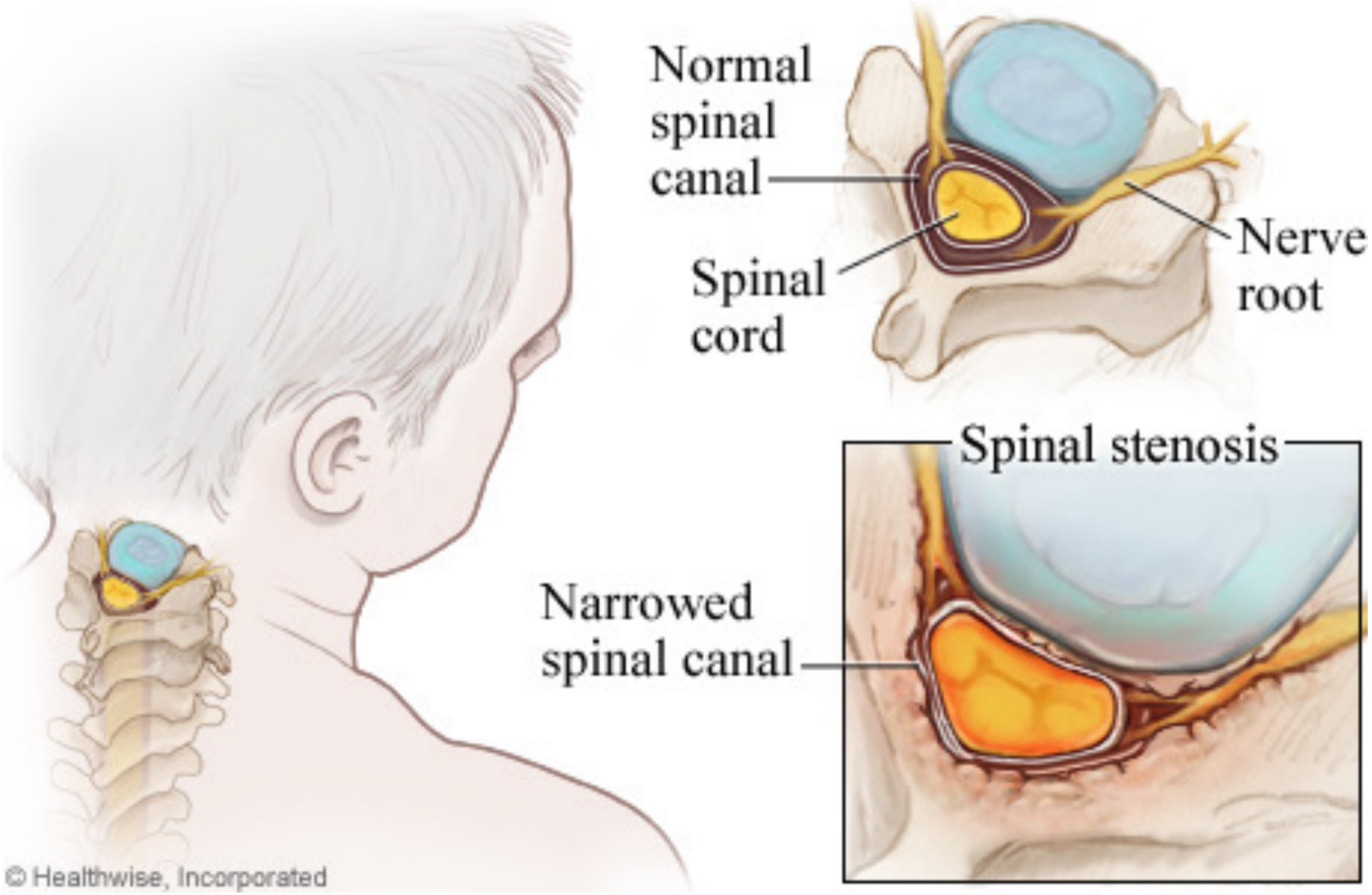
A Case Study: Spinal Implants



https://www.grandviewresearch.com/industry-analysis/spinal-implants-spinal-devices-market

A Case Study: Spinal Implants





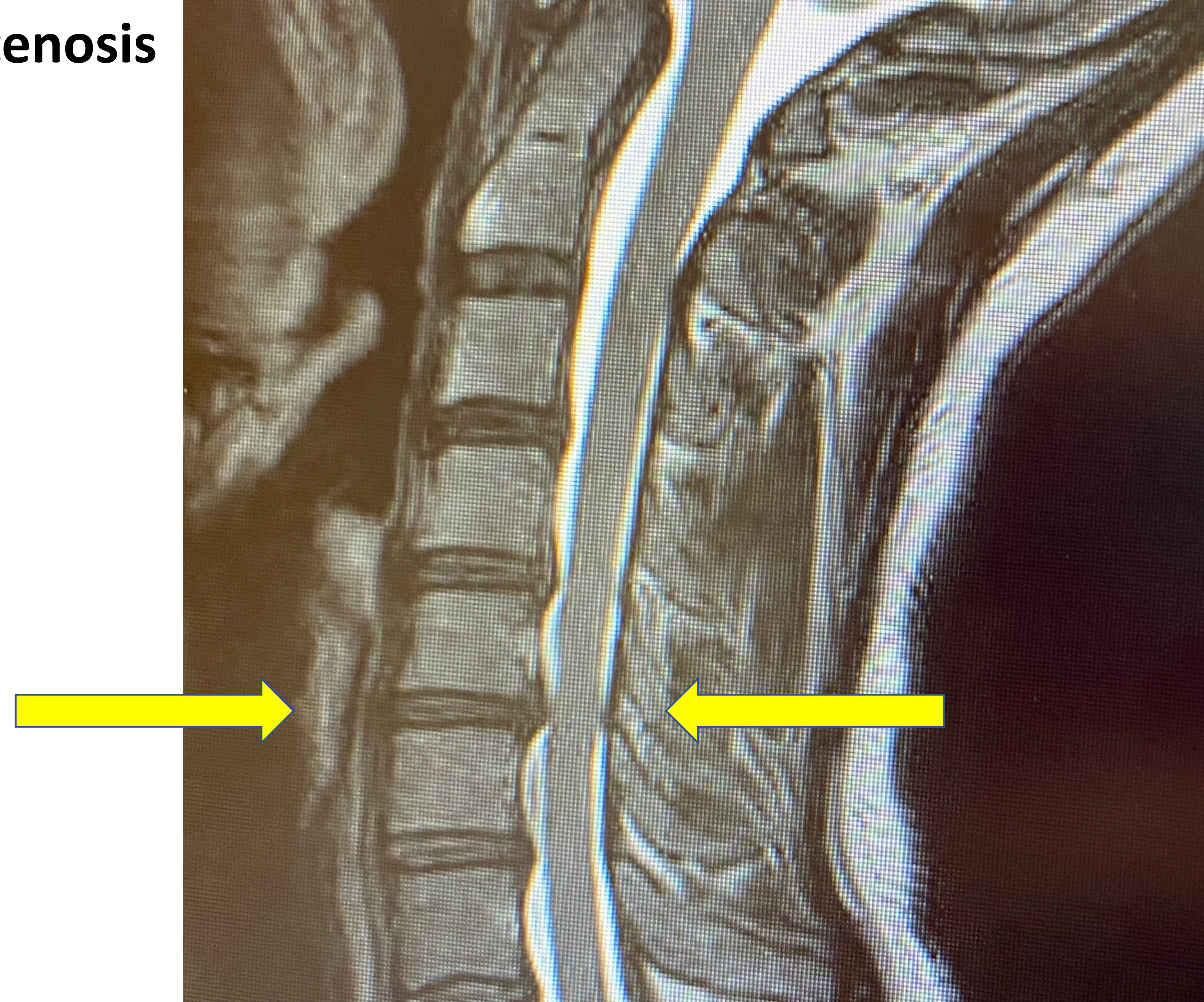
https://www.healthlinkbc.ca/illnesses-conditions/joints-and-spinal-conditions/cervical-spinal-stenosis

Clinical MRI of C5-C6 stenosis

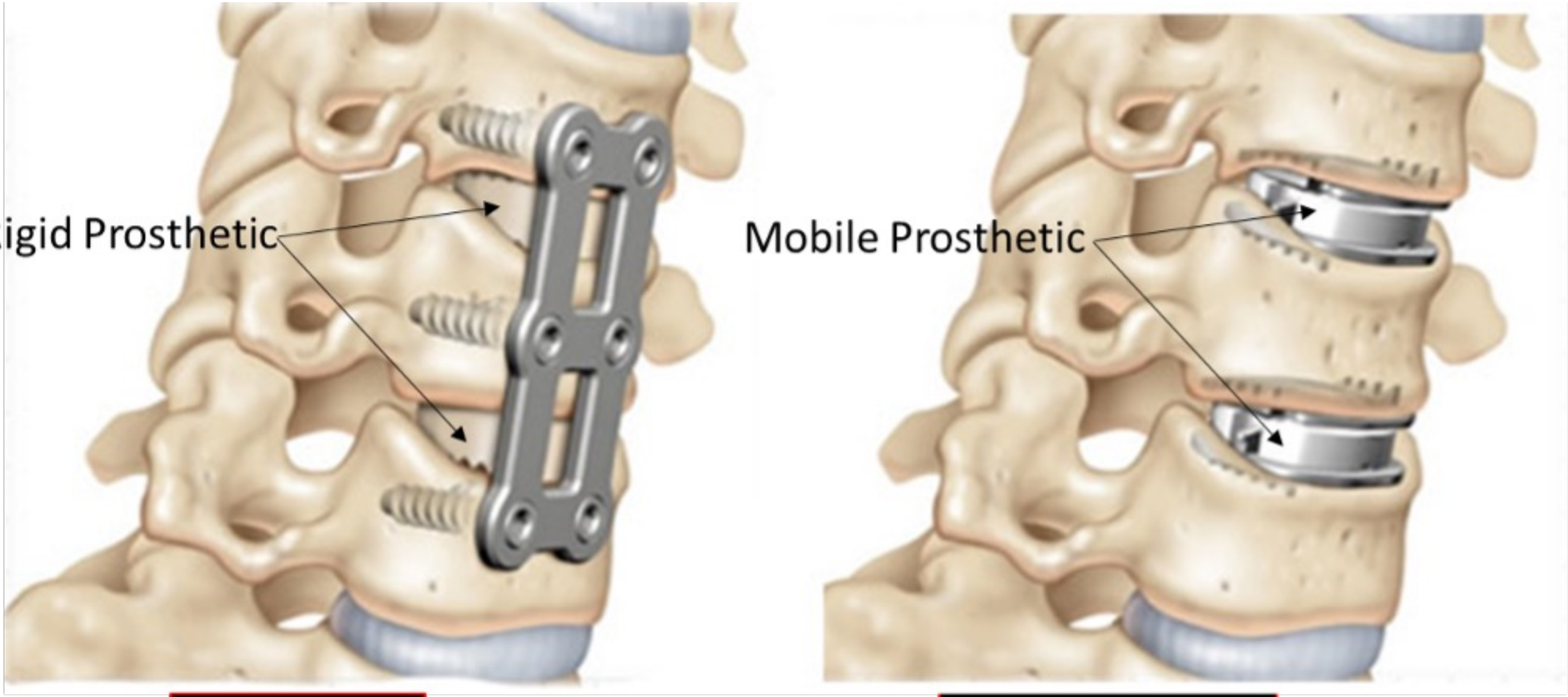
Patient 30-40y (female)

Active lifestyle

Accident with neural symptoms



Fusion or Implant?

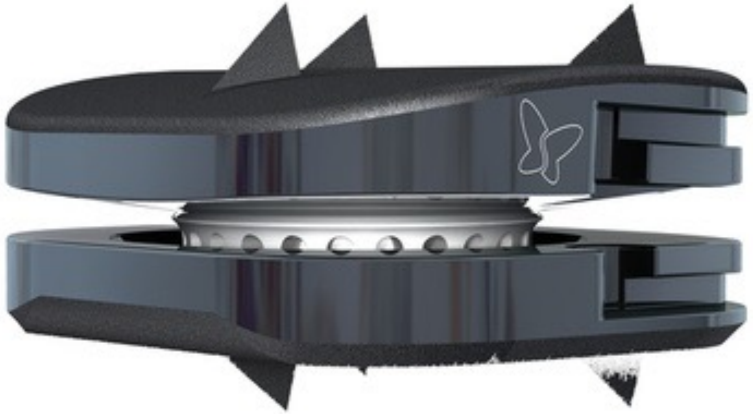


2-level ACDF

2-level Total Disc Replacement

https://www.cnsomd.com/surgery-conditions/degenerative-spine-conditions/cervical-stenosis/

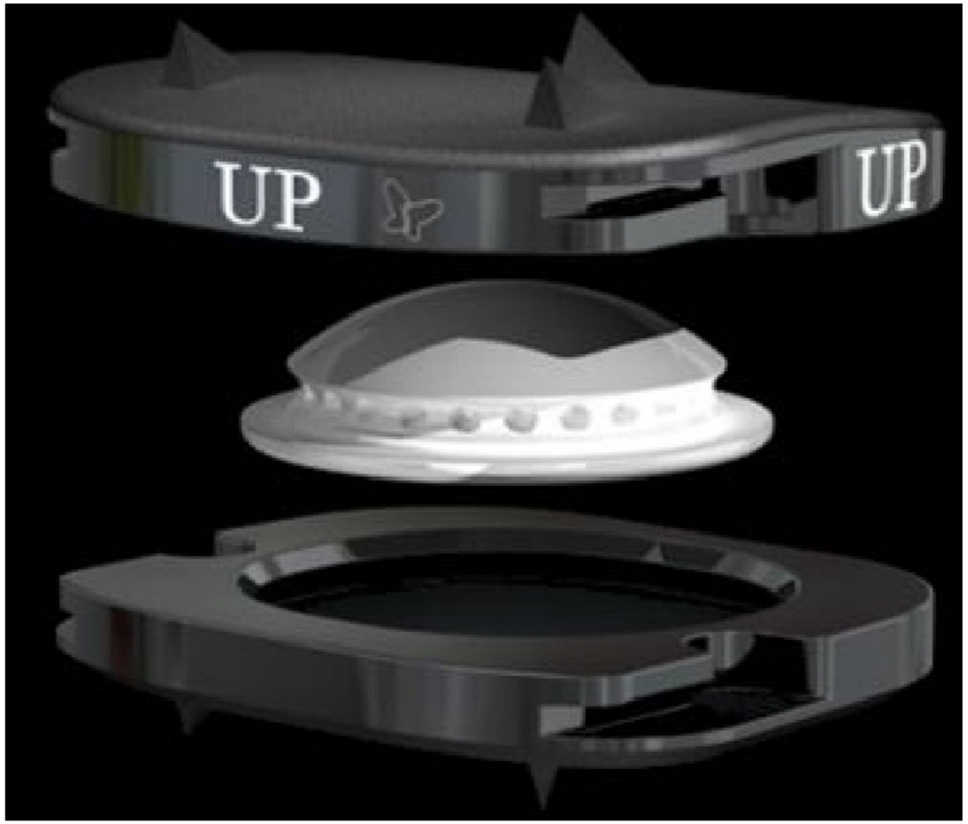
Implant



Titanium device with polymeric core

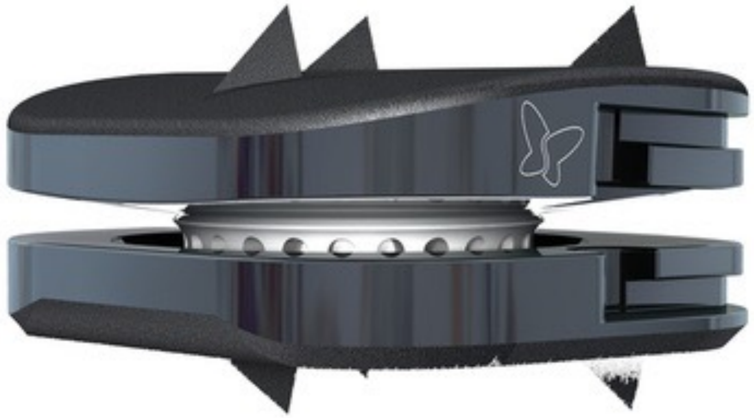
Preserves mobility in all directions

Allows for axial impact damping



:aguera C prosthesis : On the upper endplate, the surface in contact with the vertebra is anato

Implant: risks

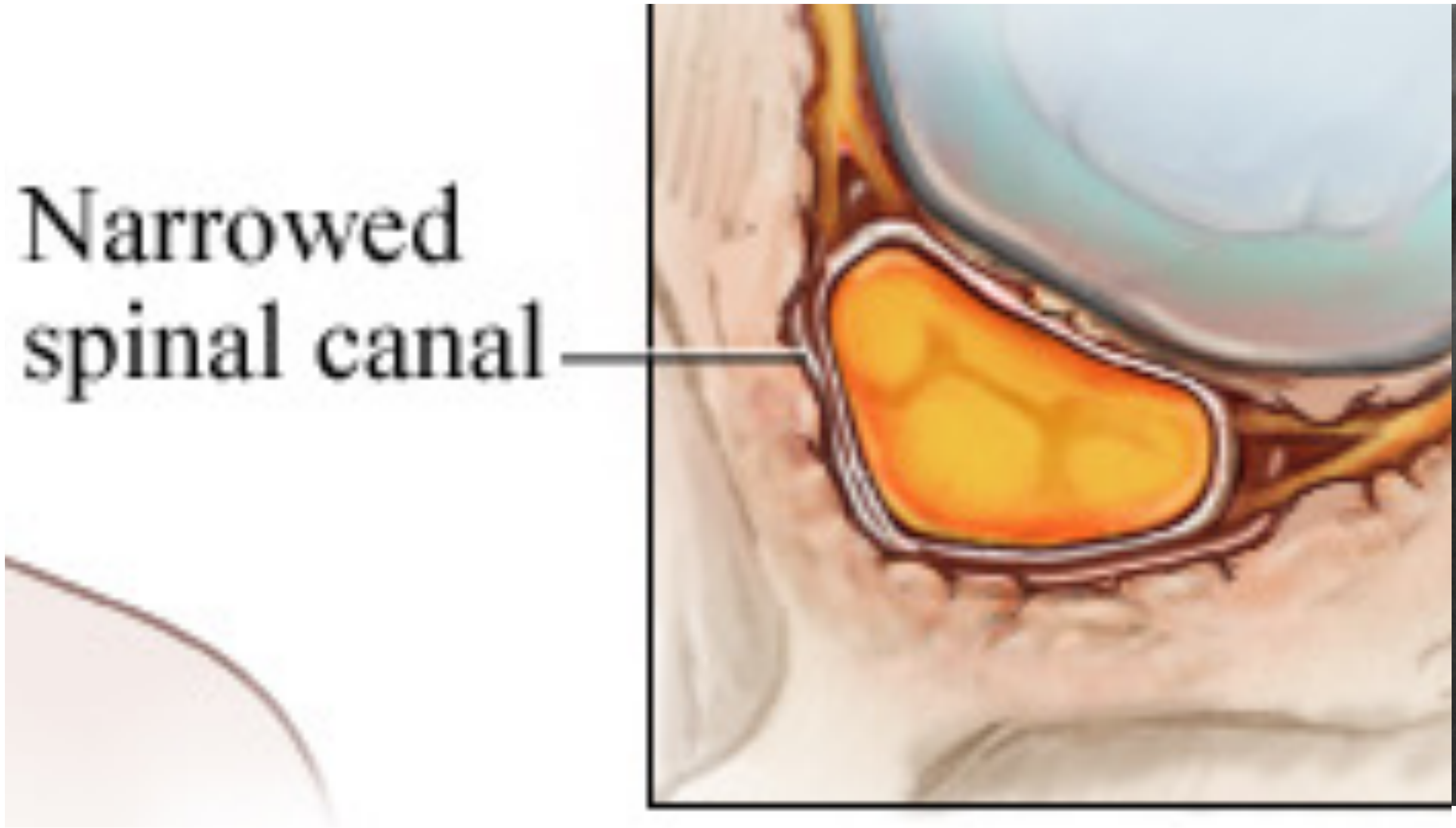


Titanium device with polymeric core

Preserves **mobility in all directions**

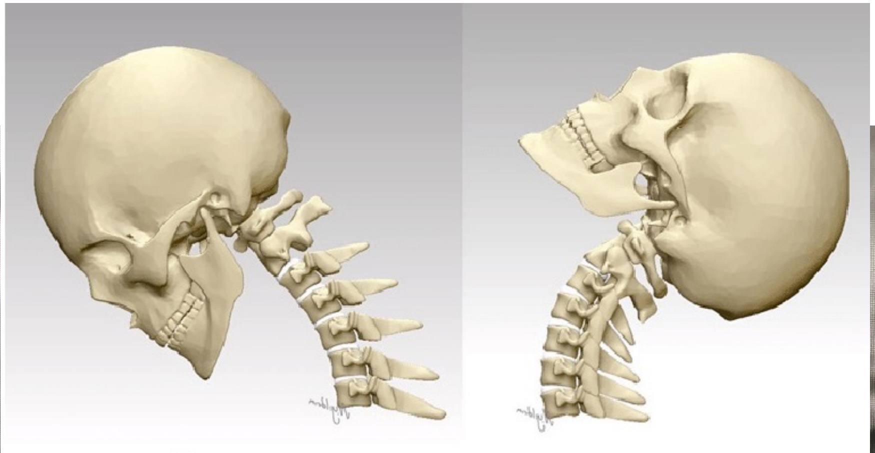
Allows for axial impact damping

Movement into spinal cord = PARALYSIS

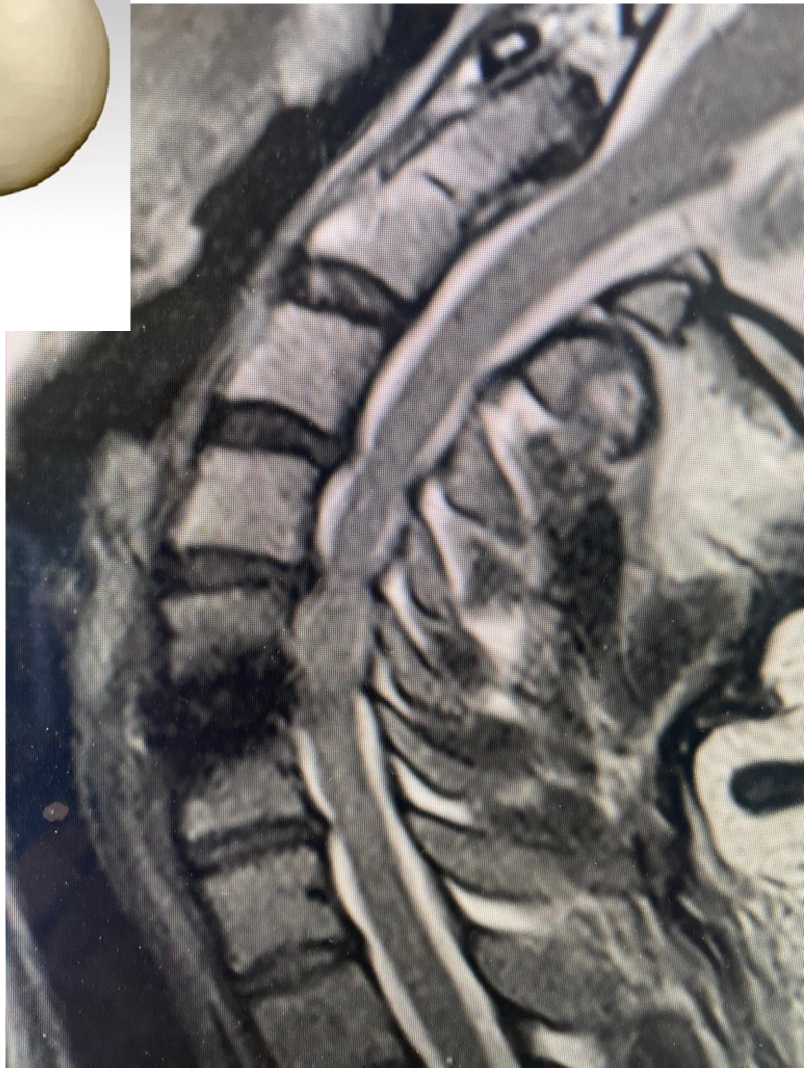


Diagnosis: Dynamic MRI

Flexion



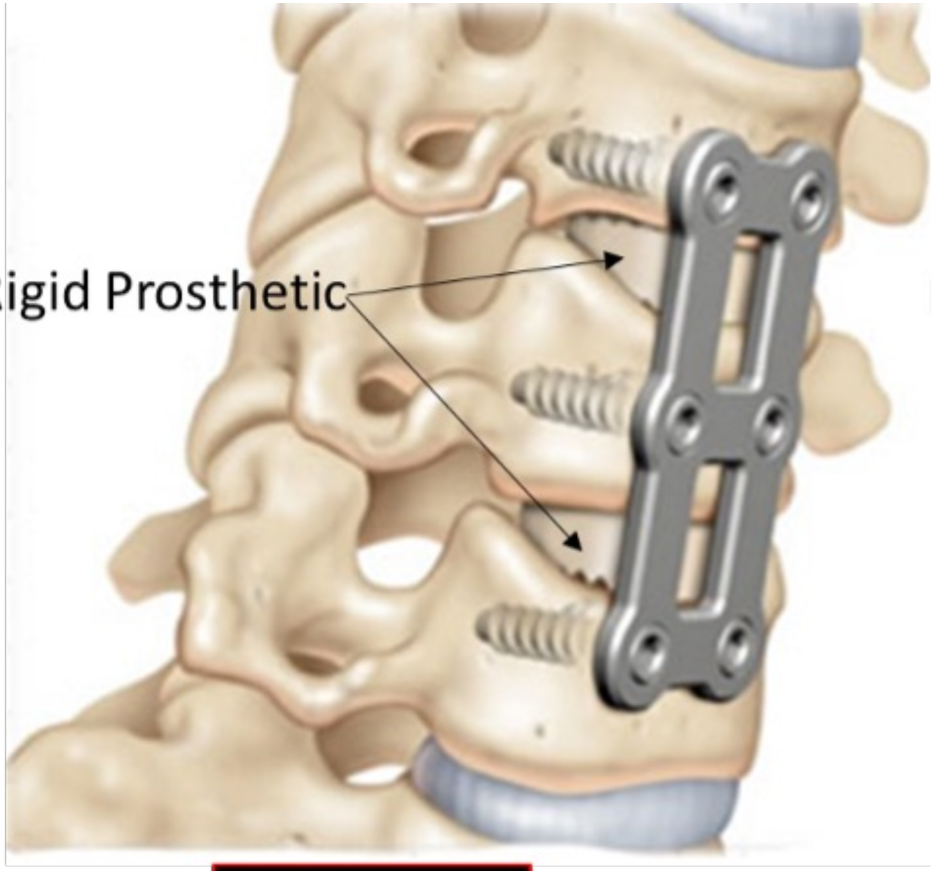
Extension



Why is implant black?

What will this patient experience?

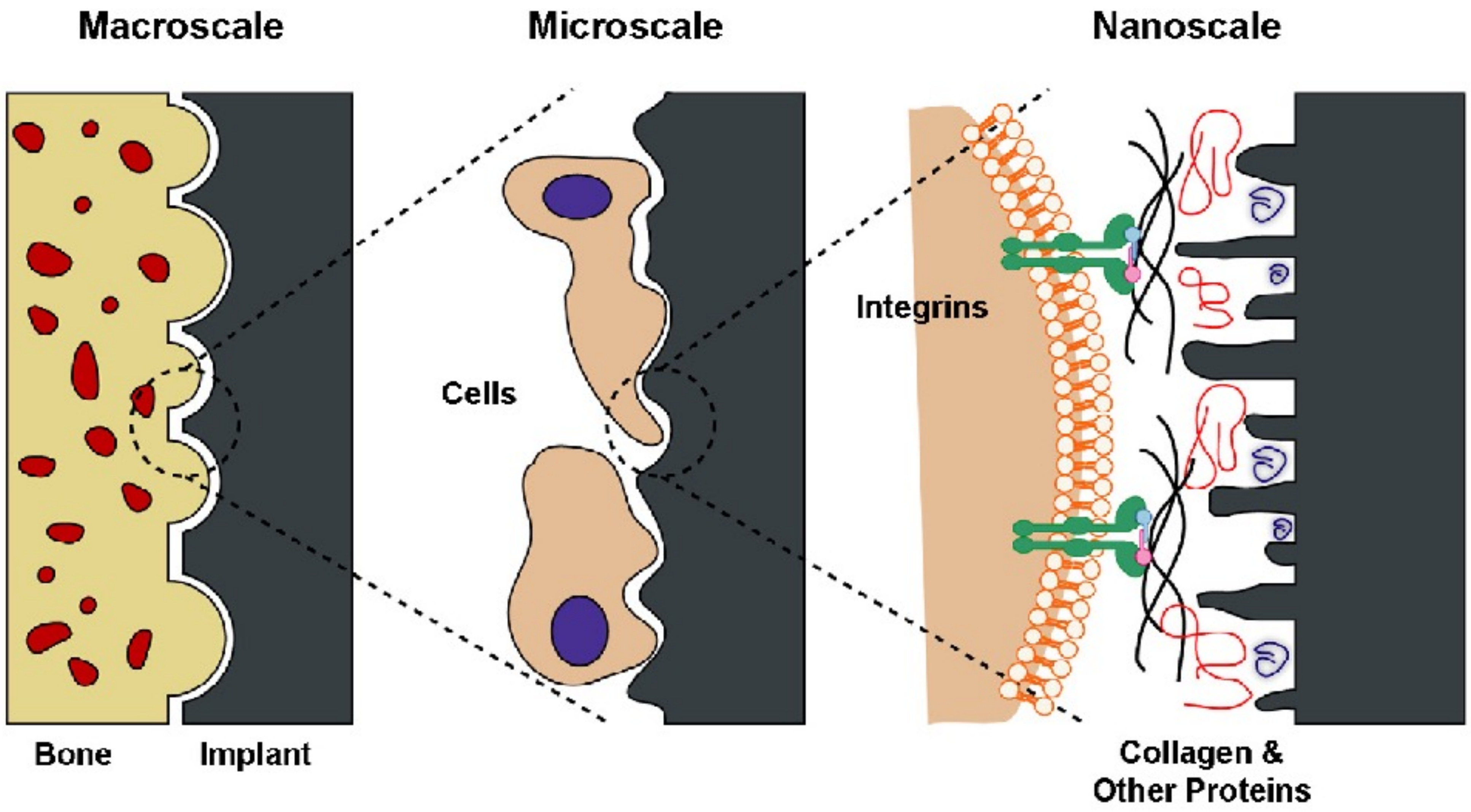
Alternative:



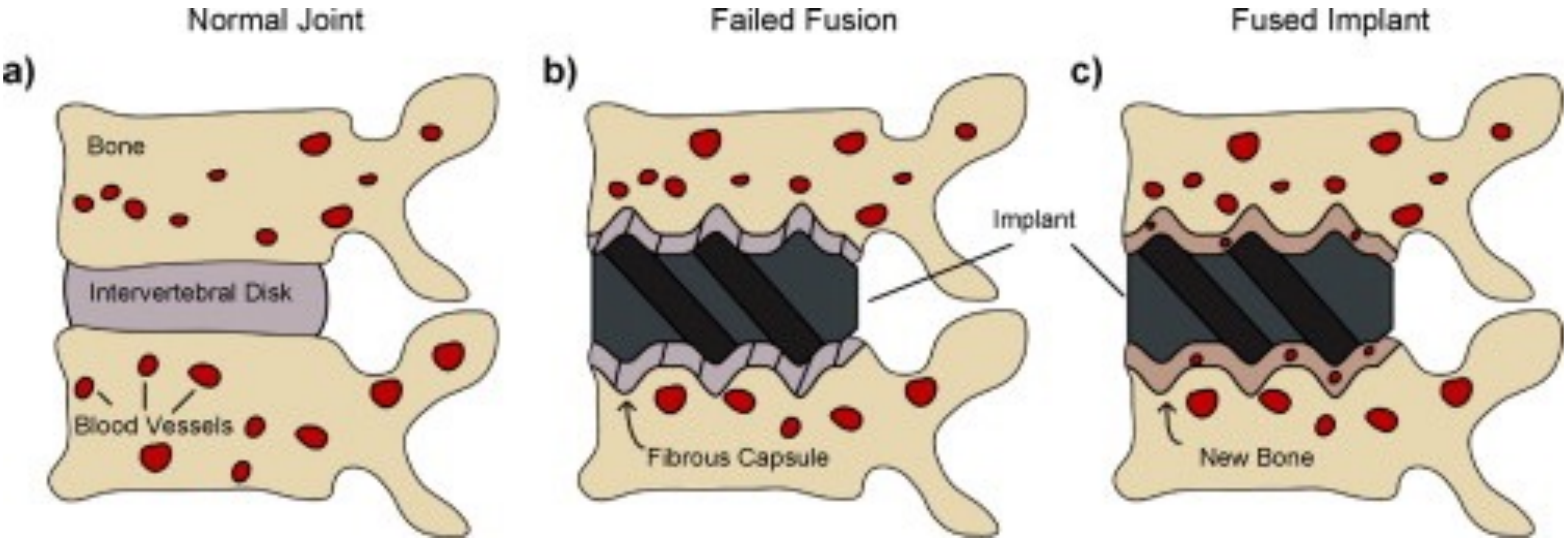
2-level ACDF

What is in the cages?

Osseointegration

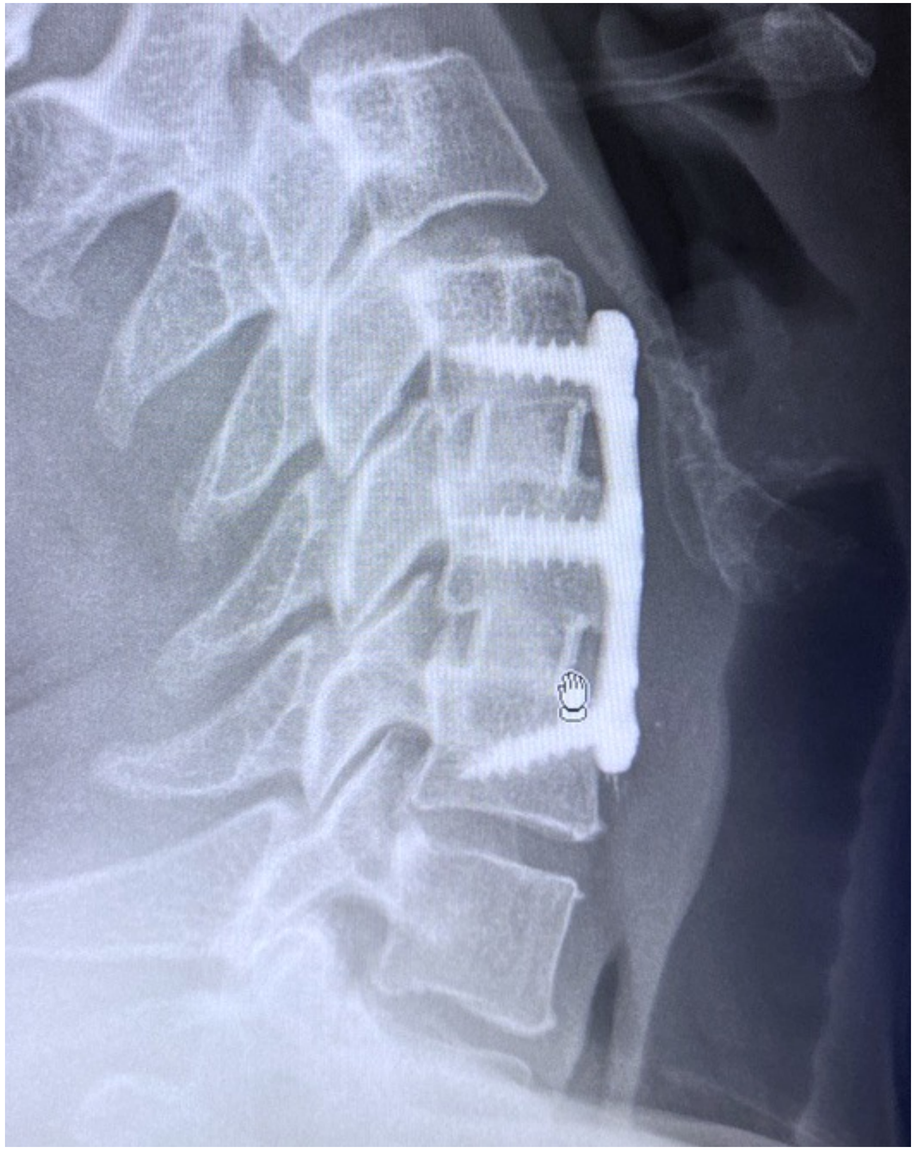


Consequences



Integration?

At surgery



1 year follow up

Conclusion

Commonly used metals are **stainless steel, titanium and cobalt**

Alloys are made to produce advantageous properties

They are primarily used in medical devices where **good mechanical properties** are needed

However, **corrosion** and **metal toxicity** are important problems

The **patient's condition** and **surgeons skills** largely impact implant success…

The ideal metal for implants is still out there…

Test Questions

A) Explain the following concepts:

- Foreign body response
- Osseointegration
- Fatigue failing
- Stress shielding

B) Place them in the appropriate time order when looking at a case of spinal implant surgery, indicate global time stamps, and explain your choice