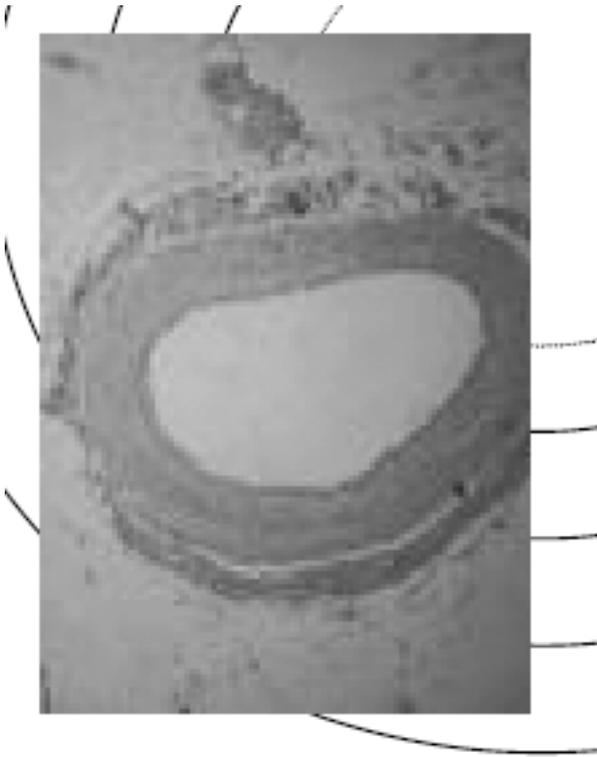
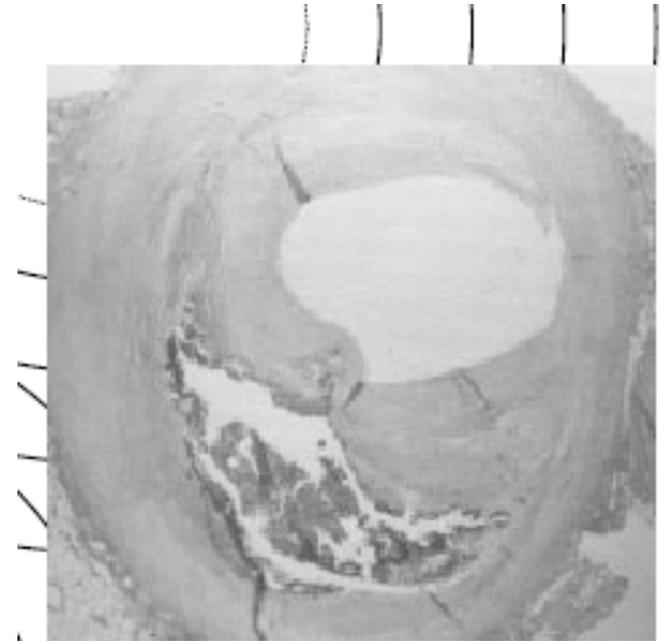


Balloon Materials in Coronary Angioplasty and Interactions Within the Vessel Wall



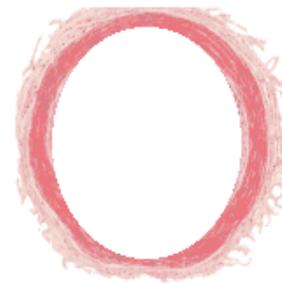
Healthy Artery



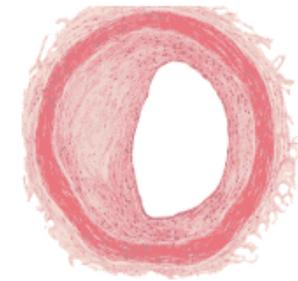
Occluded Artery

Malattie dell'apparato cardiocircolatorio

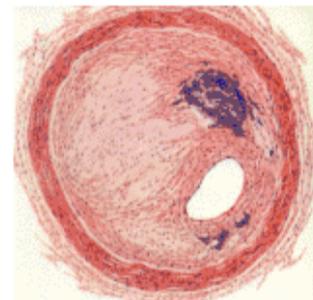
- ✓ **Arteriosclerosi:**
indurimento e
assottigliamento
delle arterie.
- ✓ **Aterosclerosi:**
forma particolare
di arteriosclerosi
che consiste nella
formazione sulle
pareti delle arterie
di placche dette
“ateromi”.



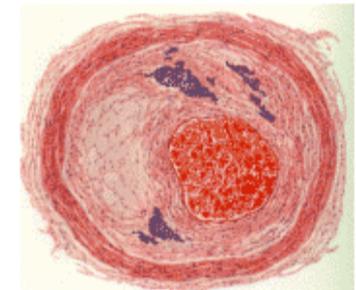
Normal Arterial Lumen



Moderate Atherosclerotic
Narrowing of Arterial Lumen

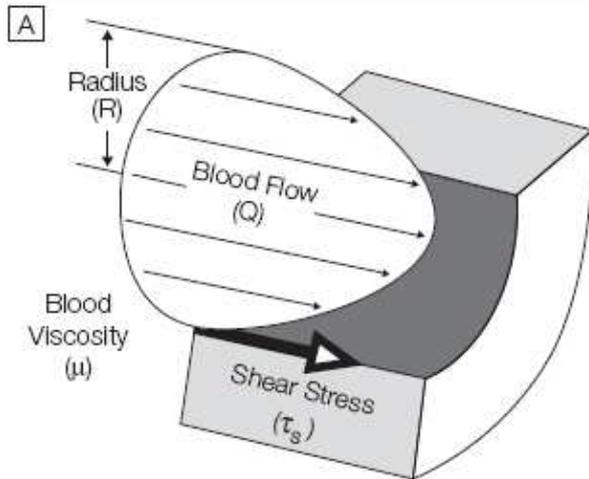


Almost Complete Occlusion
of Arterial Lumen by Intimal
Atherosclerosis with Calcium
Deposition



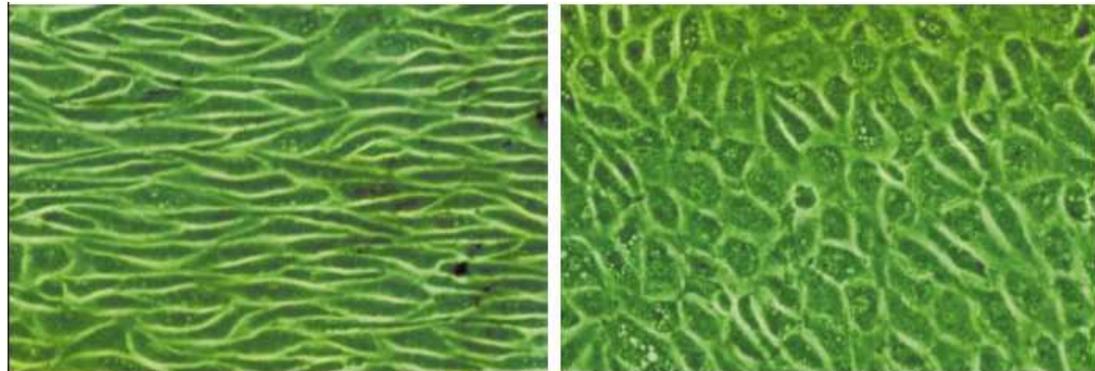
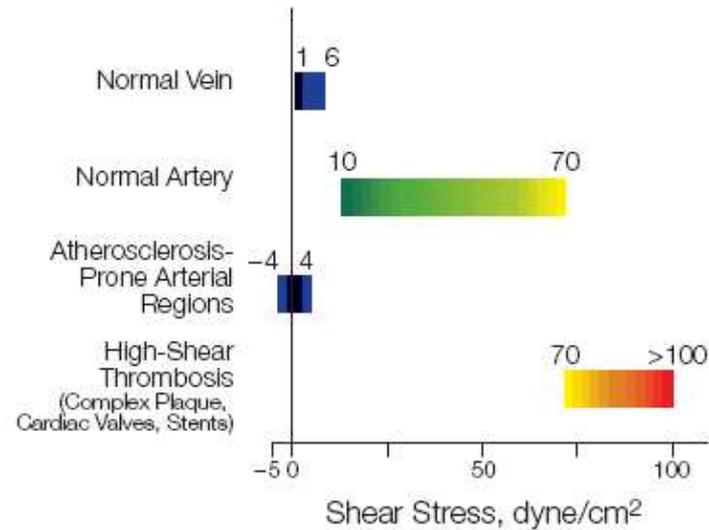
Complete Occlusion
by Thrombus in Arterial Lumen

STENT



Poiseuille's Law $\tau_s = \frac{4\mu Q}{\pi R^3}$

B Range of Wall Shear Stress Magnitude



Risposta delle cellule endoteliali

aumento della permeabilità intercellulare
 rilascio di determinati fattori che favoriscono la coagulazione, proliferazione di cellule muscolari lisce...

Percutaneous Transluminal Coronary Angioplasty (PTCA) is quickly becoming one of the most popular and common cardiovascular disease treating procedures *because of its minimally invasive, non-complex procedure and its high level of success in treating coronary atherosclerosis, or hardening and occlusion of the arteries from fatty plaque build-up and cholesterol deposition.*

More premature deaths are caused by blocking of oxygen and blood to heart than any other disease in North America, and over 2 million PTCA procedures have taken place in the past two years alone.

Balloon angioplasty procedures make use of a long catheter with a small balloon at the distal tip that is 20mm long and 3.0mm in diameter on average, although many sizes are currently available.

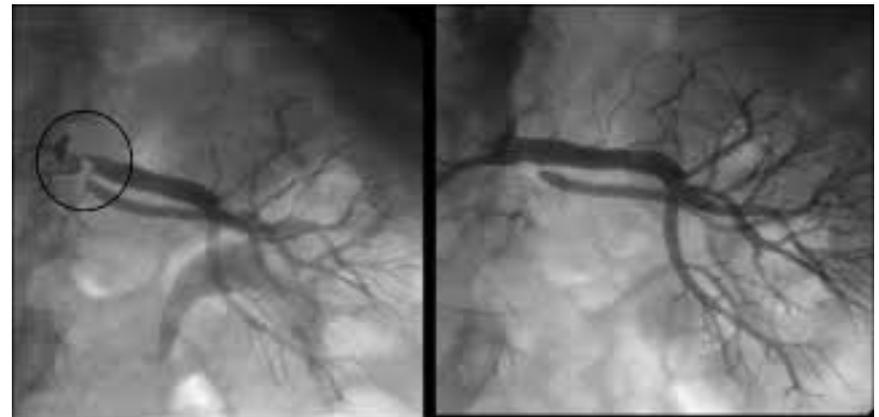
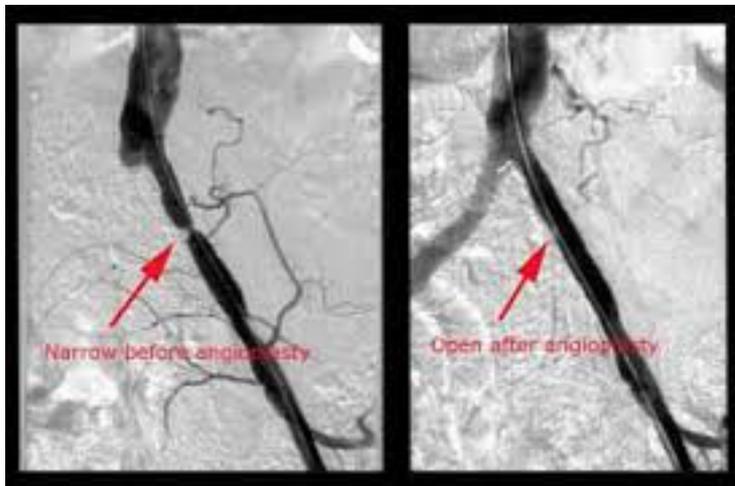
A separate guide catheter is inserted into the patient's femoral artery and fed intravenously up into the aorta just below the ostium.

A radio-opaque guidewire is then inserted into the guide catheter and fed into the occluded artery at the site of the lesion. Finally, the deflated balloon catheter is fed over the guidewire and placed within the lesion. The balloon is inflated with saline, and the plaque is pushed up against the arterial wall, widening the artery and allowing unrestricted blood flow

Balloon properties, including compliance, burst pressure, dilatation force on the artery, profile, and lesion crossability are mainly influenced by the balloon material used.

High-pressure balloons are typically made from few different materials:

- polyvinyl chloride (PVC),
- poly(ethylene terephthalate) (PET),
- high density poly(ethylene)
- polyolefin copolymer (HDPE/POC),
- nylon
- polyurethane.



Polyvinyl Chloride

The first angioplasty balloon design in the 1970's was made from flexible PVC. PVC balloons were thick-walled and could not withstand high pressures that PTCA balloons are inflated to today (**6-8 atm**). Various plasticizers were used to soften the PVC to make the balloon more useful in PTCA procedures, however PVC's thin walls and brittle nature led to the balloon's low mechanical strength. **Not used anymore**



Poly(ethylene) and Polyolefin Copolymers

In the 1980's, PE and POC balloons replaced many of the PVC balloons as a result of their ability to withstand greater pressures (**10 atm**) and have greater flexibility within the lesion. HDPE and polyolefin copolymers are cross-linked polymers that may come in several different forms. Polyolefin balloons are synthesized to form various block copolymers to obtain areas of stiffness and flexibility. Anyway the mechanical strength is low.

Poly(ethylene terephthalate)

PET balloons, introduced in the mid-1980's, provided a large step in balloon technology because of the material's compromising features. PET is a condensation polymer produced from ethylene glycol, (HOCH₂CH₂OH), and dimethyl terephthalate, (CH₃O₂C–C₆H₄–CO₂CH₃). By the process of transesterification, these monomers form ester linkages between them, yielding polyester that is typically woven in many applications. **PET is able to form balloons with very thin walls while withstanding ultra-high inflation pressures (20 atm, thickness of 5-10 micron, diameter 0.5-50 mm)**. These properties give PET balloons the ability to form a wide variety of shapes for many types of occlusions, while maintaining high tensile strength.

Nylon

Though not as mechanically strong as PET or PE balloons, the introduction of Nylon balloons in the early 1990's (Duralyn) **provided a softer balloon materials for ease of crossing the lesion and greater patient comfort**

With PET, nylon is among the most common balloon materials used today, with a reasonably high inflation pressure rating (**16 atm**) and a medium mechanical strength.

Recently, **polyurethane** has been considered as a balloon material because of its compatibility with new angioplasty techniques, such as lasers, ultrasound and microwave technology.

Polyurethane has proven to have a low-level of biological interaction problems when inserted into the body.

However, polyurethane has a lower mechanical strength in balloon applications and cannot withstand very high inflation pressures (**10 atm**).

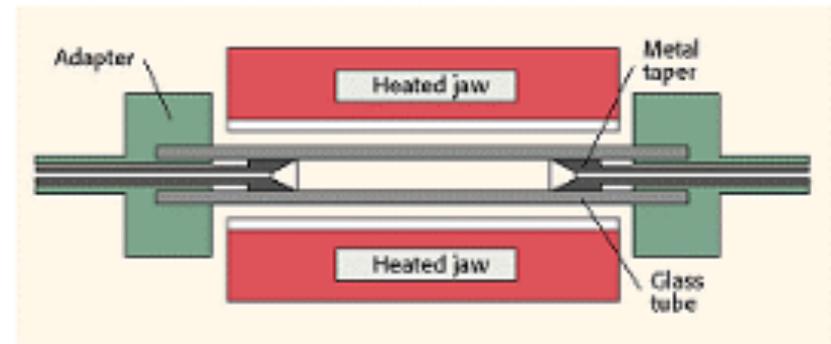
Materials	Tensile Strength	Compliance	Stiffness	Profile	Max. Rated Pressure for PTCA*		Sterilization Methods
					ATM	PSI	
PET	High-Very High	Low-Medium	High	Low	20	294	EtO or Radiation
Nylons	Medium-High	Medium	Medium	Low-Medium	16	235	EtO
PE (crosslinked) and other polyolefins	Low	High	Low	High	10	147	EtO or Radiation
Polyurethanes	Low-Medium	Medium-High	Low-Medium	Medium-High	10	147	EtO
PVC (flexible)	Low	High	Low	High	6-8	88-117	Radiation

* The maximum rated pressure is based on practical limitations and usefulness. Obviously, very thick walls can be used with any material to increase the rated pressure; however, the balloon would be useless.

I palloni per angioplastica si producono secondo un processo simile al **blow molding**.

Una preforma (tubo polimerico estruso) è inserito in una guida di vetro (*glassform*). Un'estremità viene chiusa, l'altra è collegata ad un compressore

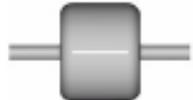
1. La temperatura esternamente alla guida viene aumentata (tipicamente 10°C-20°C al di sotto della temperatura di fusione)
2. Il tubo è mantenuto a tale temperatura a pressione interna costante per un certo tempo
3. La pressione interna si innalza
4. Il tubo viene *stretchato* fino ad ottenere la lunghezza e spessore adeguati.



KEY DEFINITIONS

Balloon Diameter:	nominal inflated balloon diameter measured at a specified pressure
Balloon Length:	typically refers to the working length or the length of the straight body section
Burst Pressure:	average pressure required to rupture a balloon; usually measured at body temperature
Rated Burst Pressure:	maximum statistically guaranteed pressure to which a balloon can be inflated without failing. For PTCA and PTA catheters, this is normally 95% confidence/99.9% guarantee
Balloon Profile:	maximum diameter of the balloon when mounted on a catheter in its deflated and wrapped condition or the smallest hole through which the deflated wrapped balloon catheter can pass
Balloon Compliance:	change in balloon diameter as a function of inflation pressure

Forme di palloni High Pressure

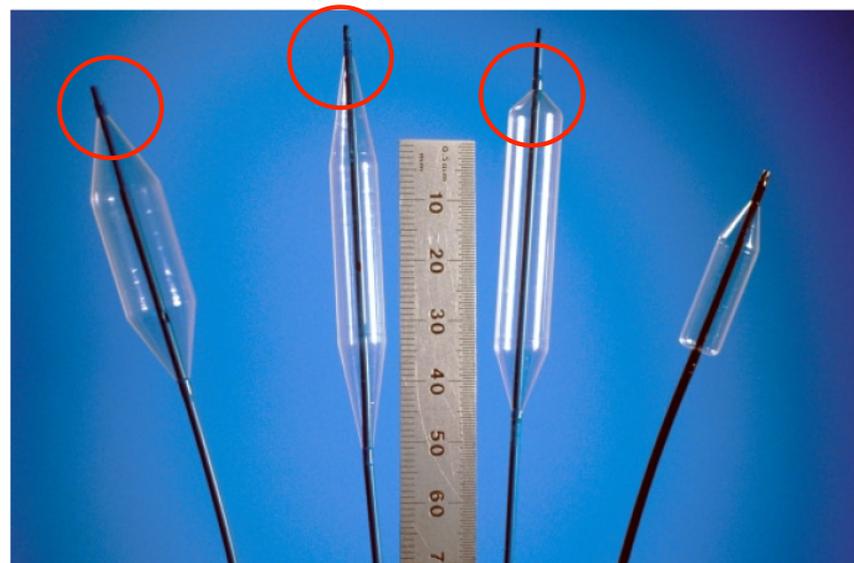
<p>Conical Balloon</p> 	<p>Square Balloon</p> 	<p>Long Spherical Balloon</p> 	<p>Tapered Balloon</p> 
<p>Spherical Balloon</p> 	<p>Conical/Square Balloon</p> 	<p>Dog Bone Balloon</p> 	<p>Stepped Balloon</p> 
<p>Conical/Square Long Balloon</p> 	<p>Conical/Spherical Balloon</p> 	<p>Offset Balloon</p> 	<p>Conical/Offset Balloon</p> 

Applicazioni di palloni High Pressure

Angioplastica coronarica: diametro 2-4 mm, lungh 10 – 40 mm.
Pressione di gonfiaggio 10-20 atm

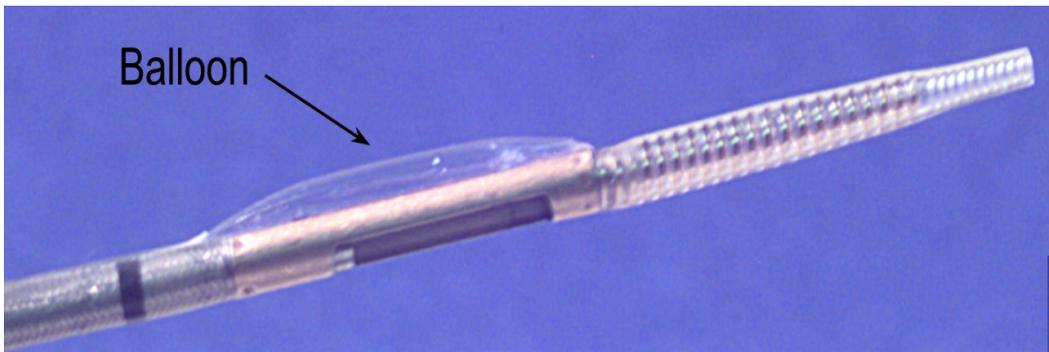
Angioplastica non coronarica: diametro 4-12 mm, lungh 20 – 100 mm.
Pressione di gonfiaggio 8-20 atm

- Esophageal dilatation
- Biliary dilatation
- Urethral dilatation
- Fallopian tube dilatation
- Heart value dilatation (valvuloplasty)
- Tear duct dilatation
- Carpal tunnel dilatation

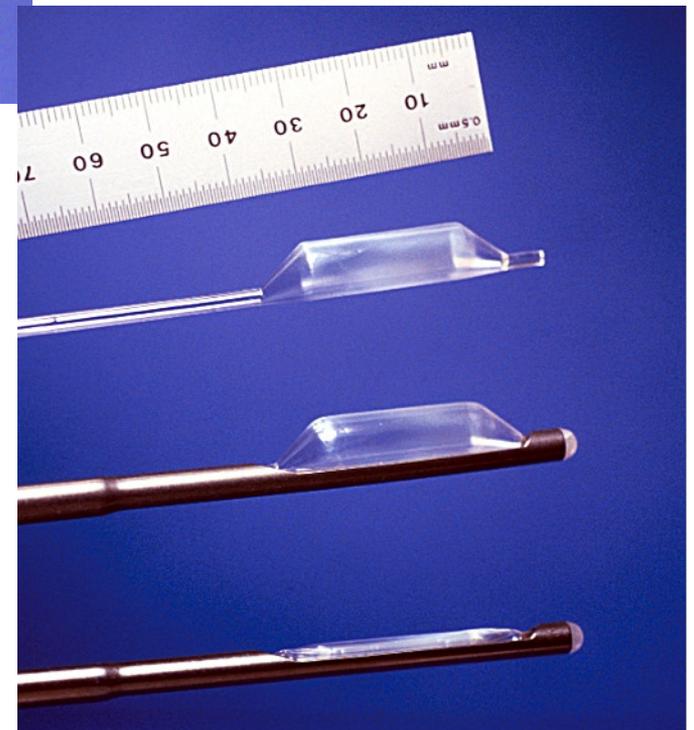


Positioning

Palloni asimmetrici servono a localizzare la forza solo su di un lato del vaso o condotto



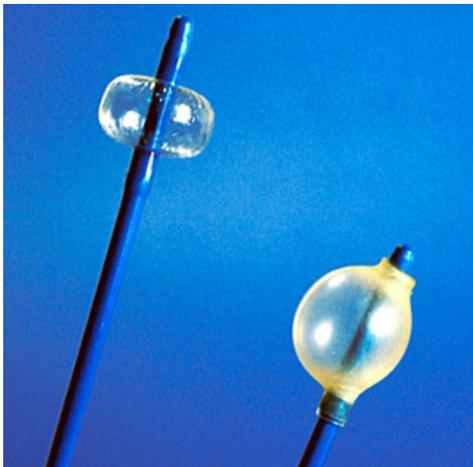
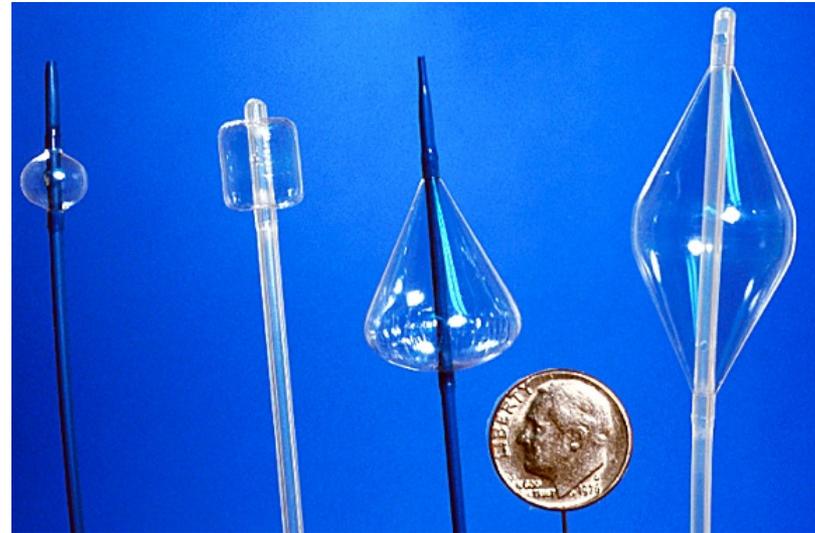
Pallone per aterectomia



Pallone per tunnel carpale

Occlusioni

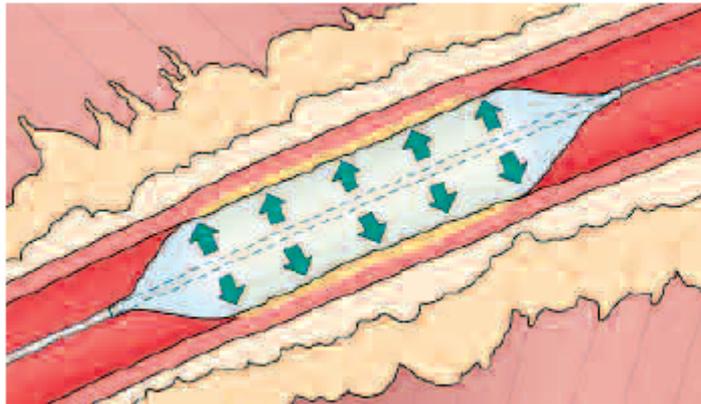
Per effettuare occlusioni di vasi o condotti, si fa ricorso a palloncini elastomerici high-compliance. Tuttavia se si devono realizzare occlusioni di specifiche dimensioni si utilizzano high-pressure, low-compliance balloons



Occasionalmente, palloni elastomerici possono dar luogo a fenomeni di instabilità e gonfiaggio asimmetrico

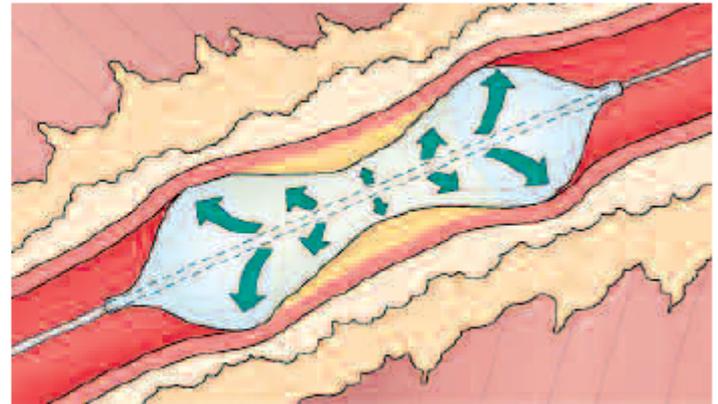
Low Compliance vs High Compliance Ballons

Non-Compliant Angioplasty



Shape retention
Greater dilating force at lesion

Semi-Compliant Angioplasty

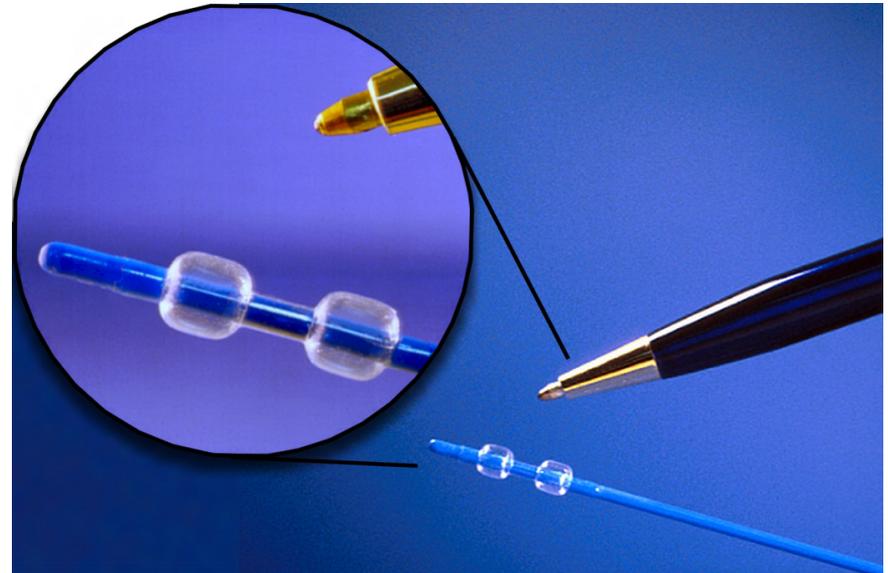
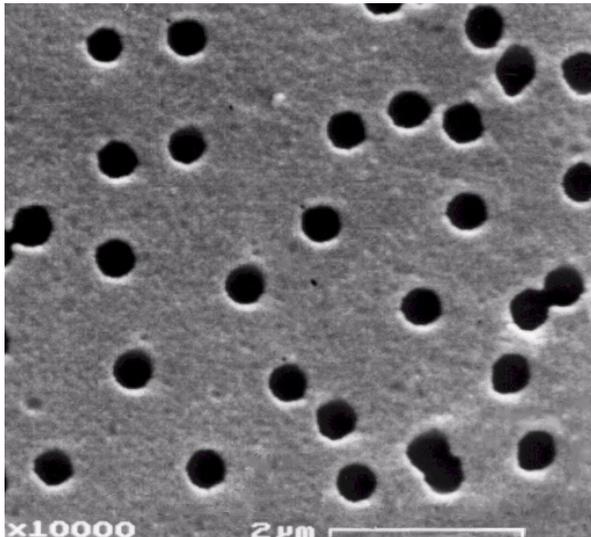


Hourglasses around lesion
Less dilating force at lesion

Rilascio di farmaci

Utilizzo di palloni a “osso di cane” per localizzare la somministrazione di farmaci ed evitare effetti sistemici.

Il farmaco viene “iniettato” nel catetere e permea attraverso le nanoporosità del materiale, pur rimanendo confinato tra i palloncini



Balloon Synthesis and Sterilization

Prior to use *in vivo*, angioplasty balloons are sterilized by either radiation procedures or ethylene oxide (EtO).

Balloons are formed by heating a specific balloon material to its glass transition temperature and melt temperature. After heating the material is highly stretched in its original balloon shape and then stretched a second time in a second direction. After cooling at room temperature, the balloon is heated again to a curing temperature to form a high polymeric orientation with enhanced structural ability.

Balloon materials are finally extruded and molded into the desired shape. Typical balloon sizes range from 1.5 - 4.0mm in diameter.

Balloon-Artery Interactions and Properties

The most important balloon properties are; compliance, dilatation force on the artery, profile, and lesion crossability.

Balloon Compliance

The compliance of a balloon material is defined as the ability of the balloon to expand in diameter at various inflation pressures. Compliance is considered the most important characterization of how a balloon will perform against the occluded lesion.

Balloon materials are usually separated into three categories based on compliance: (1) *non-compliant (NC – <5% expansion)*, (2) *semi-compliant (SC 5-10%)*, and (3) *compliant (18-30%)*.

Non-compliant balloons will maintain size and shape when inflated at high pressures, while more compliant balloons will expand beyond their predicted shape and fit lesion eccentricity.

For the past decade, there has been considerable debate as to what level of compliance is ideal for a given lesion, which will lead to new technologies in balloon material development.

POC balloons are the most compliant balloons, changing 14% in diameter when inflated between 6-10 atm pressure, while PET balloons are the most non-compliant, changing only 3%. PE, Nylon, PVC and polyurethane range in the middle with an 8-10% change.

Dilatation Force on the Artery Wall

Knowledge of the force and stress that a balloon places on an arterial wall is vital to a successful procedure and preventing injury. If a balloon exerts the right amount of cylindrical stress on the lesion, the occluded portion of the vessel is dilated to equal the radius of the non-diseased adjacent artery.

However, if a SC balloon inflates around the lesion, “dog-boning” occurs, putting the greatest amount of balloon force on the healthy surrounding artery wall, often rupturing the vessel or destroying the balloon in the body. These balloon failures can cause severe medical complications.

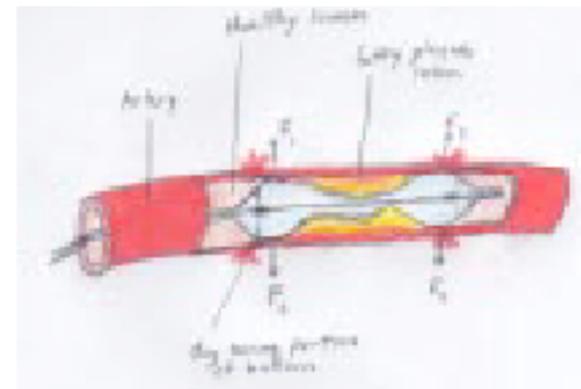


Figure 5: Dog-boning occurring against the healthy arterial wall

Inflated balloons exert two forces along its shape.

The first force, called *hoop or radial stress* (σ_r), is defined as balloon pressure (p) times balloon diameter (d) divided by two times the balloon wall thickness (t), or

$\sigma_r = p d/2 t$. This force is exerted along the radius of the lesion or artery wall.

The second force, *axial or longitudinal stress* (σ_l), divides pressure and diameter by four times the wall thickness, or $\sigma_l = p d/4 t$. Longitudinal force is exerted along the length of the inflated balloon.

SC balloons, such as POC and PVC balloons typically have a higher failure rate and dog-boning in the artery. NC balloons (PET) rarely fail in this manner, having a greater radial tensile strength (TS), which is defined by an equation identical to radial stress.

Since longitudinal stresses are often higher than radial stresses, balloon splitting usually occurs down the length of the balloon rather than the radius, which is preferable.

Balloon Profile and Lesion Crossability

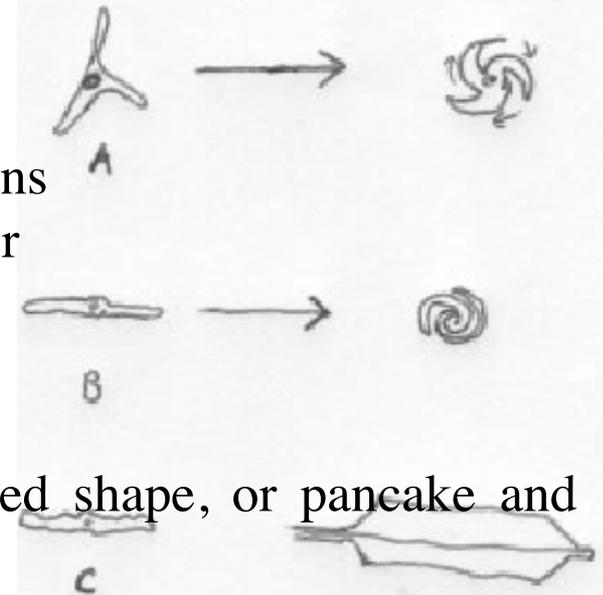
The profile and crossability of a balloon can be defined as a balloon's maximum diameter when "wrapped" around its catheter and deflated or the

smallest artery space that a balloon can pass smoothly. Although catheter pushability and trackability can be important factors in how a balloon may cross a torturous lesion and "recross" through the artery following the procedure, the balloon material is the greatest contributor to how smoothly a deflated balloon can pass a highly occluded lesion.

Prior to inflating the in the body, the balloon is folded to give a low profile before inflating.

Often the balloon is folded in two different orientations

- (1) tri-folded flaps that fold over in a circular manner
- (2) and (2) two flaps folded around each other.
- (3) After the balloon is inflated and then deflated
- (4) in the body for removal of the balloon catheter,
- (5) the balloon may either obtain its original folded shape, or pancake and "wing".



pressure is removed from the balloon, the “pancake” is the more common scenario, creating a considerable dragging profile that is more difficult to remove and “recross” the lesion with. This dragging can rupture the endothelial lining of the artery and cause medical complications. **Therefore the softness and profile of the balloon material is the key to preventing these problems.**

Although PET balloons have the lowest profile while crossing the lesion in the folded form, they are also the balloons that are most likely to pancake upon recrossing the lesion.

Nylon and Polyurethane balloons typically have low to medium profiles, while SC balloons such as PVC and PE/POC tend to have higher profiles because of their high level of flexibility.

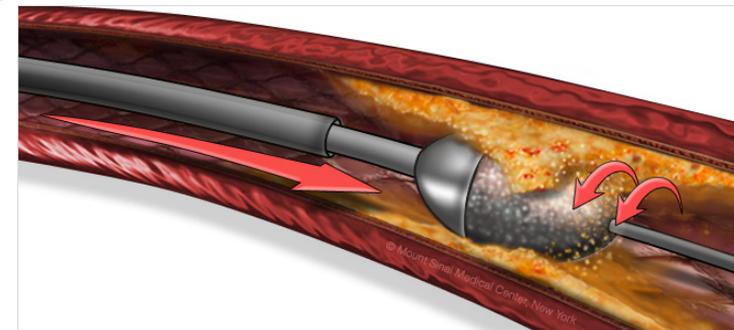
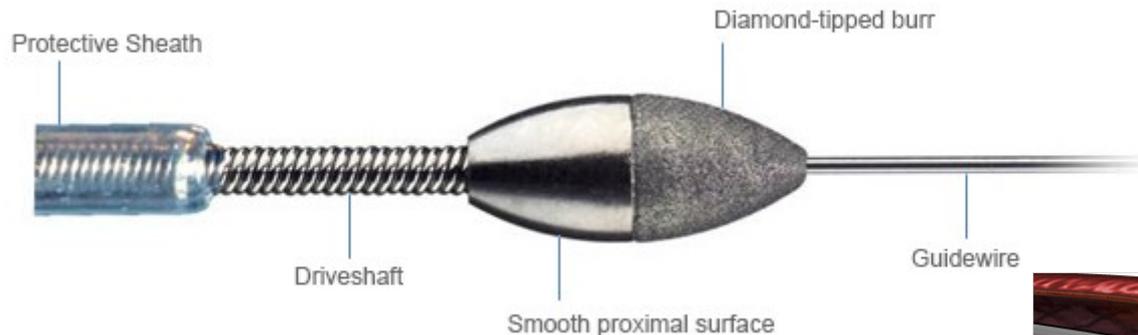
In the last few years, however, medical device companies have created wrapped balloons with a “memory” system, to increase the chance of the inflated balloon to return to its original position.

Altre tecniche

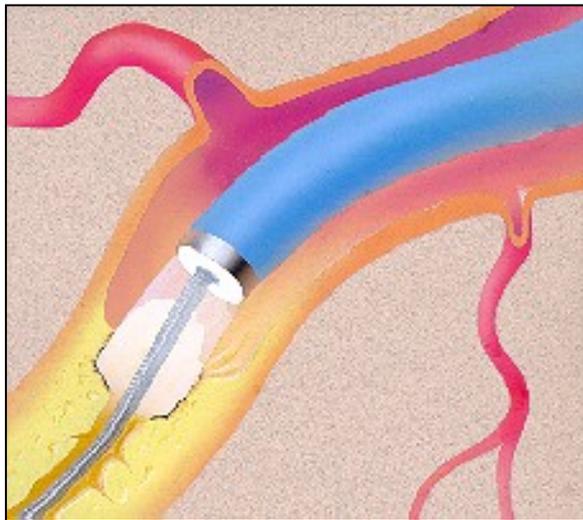


L'aterectomia rotativa (Rotablator) è una tecnica che non agisce meccanicamente sulla placca in modo da spingerla verso la parete del vaso, ma provvede alla rimozione della stessa mediante fini schegge di diamante (30-50 micron), incastonate sulla superficie di un ellissoide metallico (diametro variabile tra 1 e 2.75 mm); messo in rotazione da un albero rotante ad elevata velocità. che passa al suo interno.

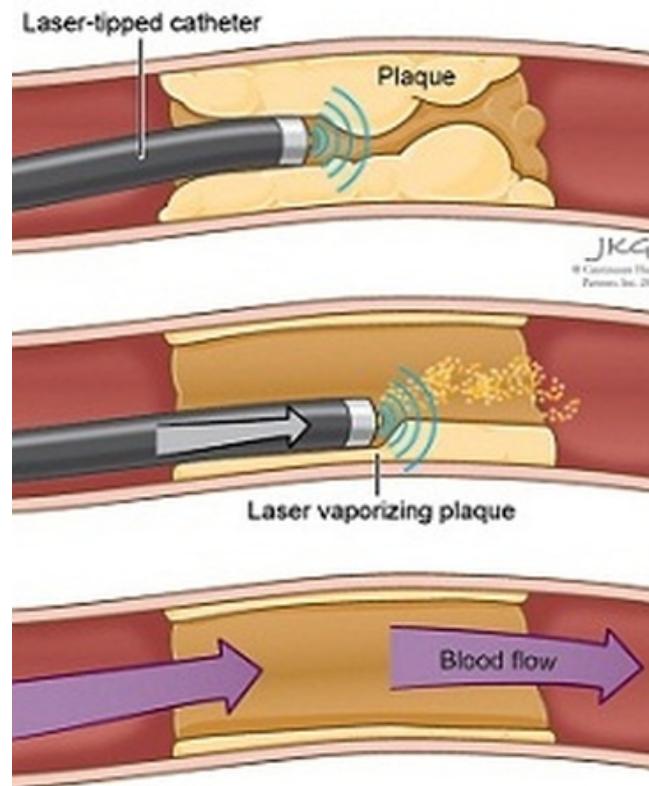
La placca viene così ridotta in minuti frammenti ben sopportati dalla circolazione sanguigna.



Altre tecniche



Infine l'**angioplastica laser** utilizza una luce monocromatica prodotta da un laser che viene concentrata su una zona molto ristretta. Si ottiene così l'ablazione diretta del materiale della placca.



Future Technologies in Balloon Angioplasty

In response to the desire combine the best properties of each balloon material and to minimize biological or stress interactions within the artery, a series of future technologies in balloon production are being researched including:

Hinged compliance balloon technology and focal angioplasty, Nitric oxide delivery, and surface modification with hydrogel IPNs.

Hinged Compliance and Focal Angioplasty Balloons

An ideal balloon is one that has a high level of compliance, high burst pressure, low-failure in dilating the artery and high tensile strength. Although one kind of balloon cannot perform at all of these levels, it is now possible to create a hinged compliance balloon or a balloon that combines both compliant and non-compliant balloon material.

This can occur by either layering NC and SC materials in a concentric form, to obtain both characteristics or by creating a balloon that has NC ends and a SC body, as in a procedure called “focal angioplasty” to better suit the lesion at a focal point.

Nitric Oxide-generating Polymers

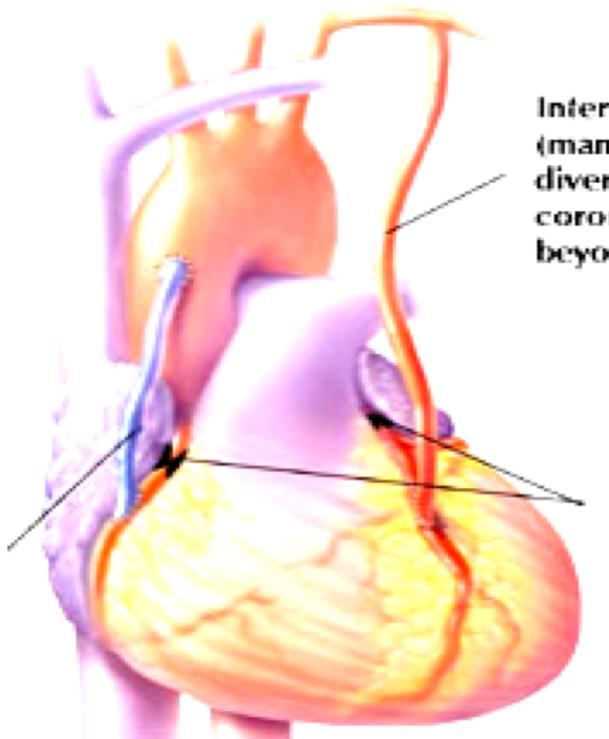
Two major complications in balloon angioplasty involve restenosis, or re-occlusion of the wall. When the vessel is dilated during balloon inflation, some endothelial lining is removed and exposed to circulating blood. This action initiates platelet adhesion and other healing events that result in the high levels of restenosis.

Recently, polymers that release nitric oxide (NO) via a hydrogel structure have been developed, which have shown to inhibit smooth muscle growth and prevent platelet adhesion and thrombosis that leads to restenosis.

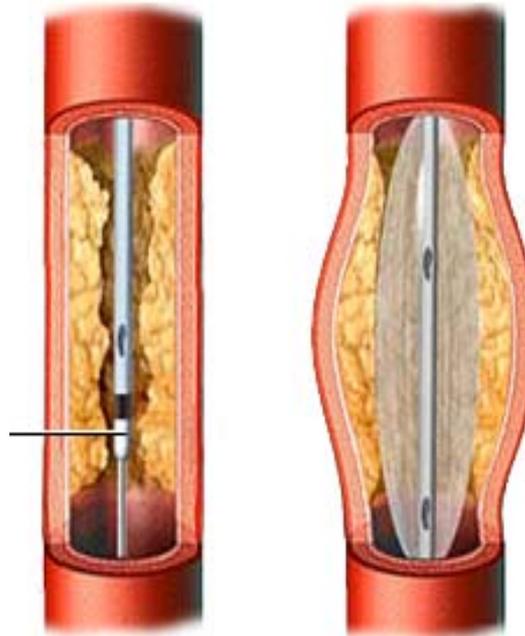
Surface Modification With Hydrogel IPNs

In the effort to enhance crossability and re-crossability of the lesion and artery, interpenetrating networks (IPNs) of poly(acrylamide-co-ethylene glycol) P(AAm-co-EG) were grafted covalently to PET balloons to increase hydrophilicity and lubricity at the balloon surface. PEG networks were grafted into the polyacrylamide network by swelling and “interdiffusion” of the PEG monomer and cross-linker by photo-initiation radiation techniques.

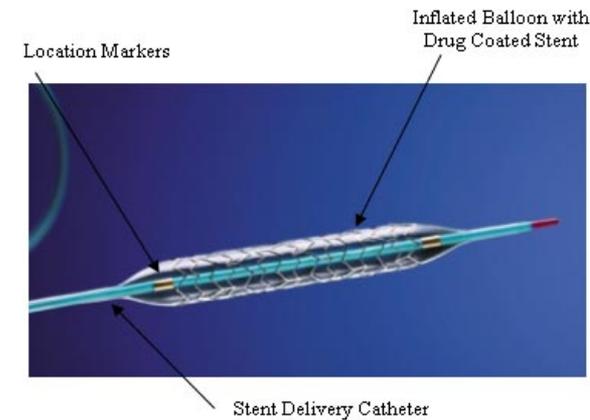
Come intervenire?



By-pass



Angioplastica



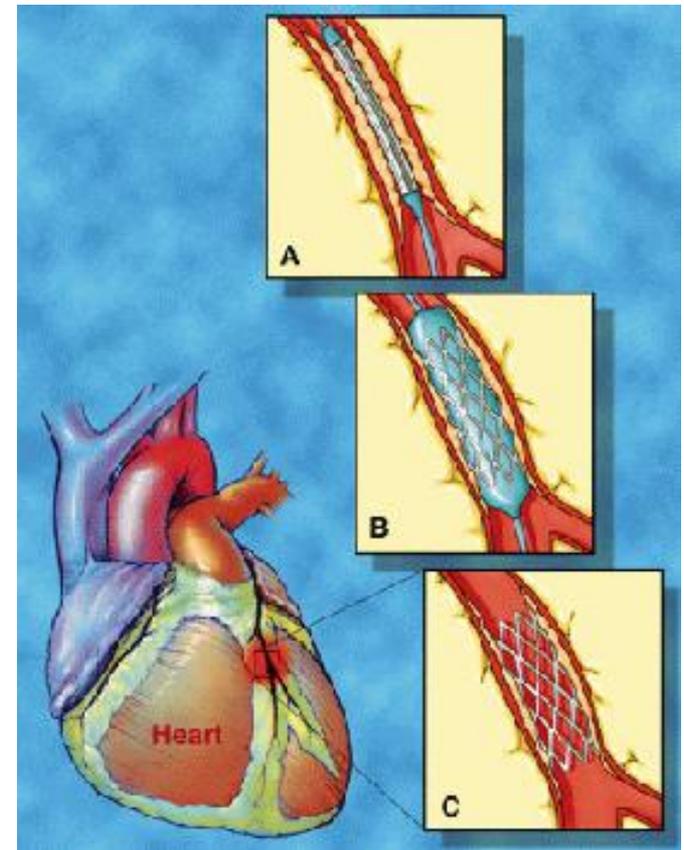
Stent

Stent Production Overview

- 460,000 Stent procedures performed in the United States in 2000.
- However, the Big 4 are highly secretive about their production methods.
- Many stents are produced by numerous smaller production facilities

Cos'è uno stent?

Lo stent è una reticella metallica a configurazione tubolare collocata tramite un palloncino sgonfio nel tratto ristretto del vaso dove successivamente viene distesa e lasciata mediante la dilatazione del palloncino, gonfiato ad alta pressione. Lo stent in questo modo sostiene le pareti coronariche evitando che si possano restringere nuovamente.



Vantaggi:

- Riduce le complicazioni immediate rispetto all'uso del palloncino;
- Consente di dilatare anche stenosi più dure;
- Mantiene più frequentemente aperti i vasi che dopo la dilatazione con il palloncino potrebbero tendere a restringersi.

Problemi:

- Ristenosi, ossia la riocclusione dei vasi (anche se dimezzata rispetto all'uso del palloncino);
- Trombosi;
- Irritazioni e infiammazioni che a lungo termine inducono la formazione di nuova placche;
- Migrazione dello stent.

Materiali

I materiali per stent devono avere le seguenti caratteristiche:

- Biocompatibilità;
- **Resistenza alla corrosione;**
- Resistenza alla fatica;
- Non trombogenicità;
- Capacità di sostegno;
- Visibilità ai raggi X;
- Elevato modulo elastico (minimo recoil)
- Basso limite di snervamento;
- Resistenza a pressione e torsione

Tecnologie di fabbricazione

Un tipico stent coronarico ha **spessore variabile tra 0.056 mm a 0.2 mm**, **diametro interno prima dell'espansione da 0.99 mm a 1.15 mm**, e dopo espansione, il diametro esterno e la lunghezza possono raggiungere rispettivamente valori da **2 mm a 6 mm** e da **7 mm a 45 mm**.

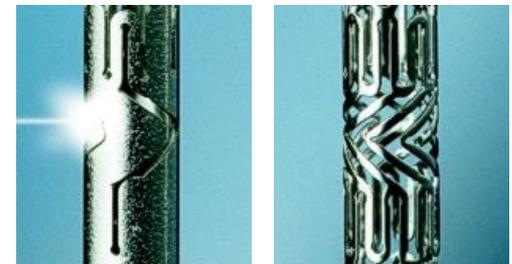
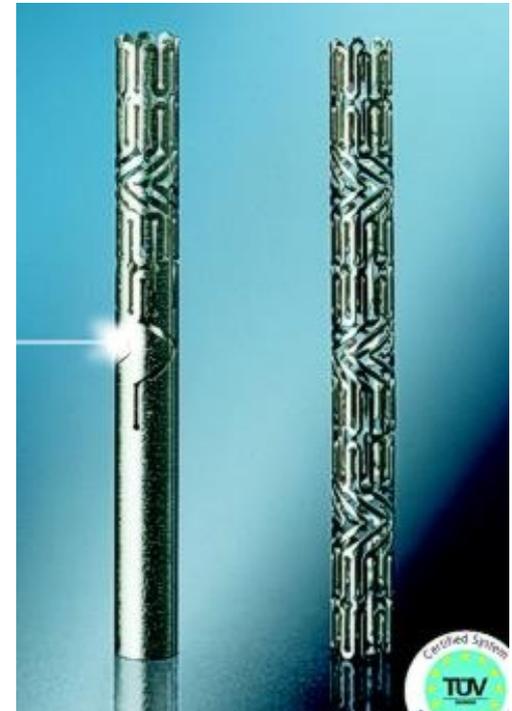
Il materiale può essere lavorato in due modi diversi:

- viene prodotta una serie di **fili metallici sottilissimi** (fino a 0.076 mm di diametro), che vengono poi disposti elicoidalmente e così **brasati o saldati**, con il risultato di ottenere una struttura reticolare (tecnologia piuttosto costosa)

- si ottengono per estrusione tubi cavi metallici dalla parete molto sottile** (fino a 0.056 mm di spessore), successivamente intagliati con tecnologia di taglio laser, ottenendo direttamente la geometria desiderata, senza bisogno di giunzioni meccaniche o termiche.

- Le endoprotesi tubulari** hanno come principale vantaggio la loro grande forza radiale, a spese di una flessibilità limitata. Le loro indicazioni sono le placche calcificate o i segmenti di arteria retti.

- Le endoprotesi modulari** hanno una maggiore flessibilità, a spese della loro forza radiale. Esse sono adatte alle zone molto angolate e alle zone di biforcazione, ma sono meno efficaci nelle lesioni calcificate



Criteri di scelta: **Meccanici**

- **Trackability:** rappresenta la facilità di manovra degli stent nelle tortuosità arteriose.
- **Conformabilità:** è la capacità dello stent di adattarsi all'anatomia della lesione.
- **Flessibilità** (caratteristica molto importante per le arterie sottoposte a delle deformazioni importanti) e
- **Resistenza allo schiacciamento**, o forza radiale (resistenza a una compressione esterna in direzione radiale):

NB la flessibilità va a scapito della forza radiale.

- **Il ritorno elastico** (recoil) rappresenta la riduzione di diametro dello stent dopo il posizionamento. È auspicabile che sia il più ridotto possibile
- **Geometria della mesh:** a parità di materiale e di area totale di contatto tra stent e parete del vaso, **un numero maggiore di incroci tra le maglie** della struttura aumenta la probabilità di ristenosi, poichè il vaso risulta maggiormente traumatizzato.
- **Spessore:** osservazioni cliniche hanno messo in evidenza come stent ad elevato spessore promuovano la ristenosi. Dunque al momento ci si orienta su **spessori compresi tra 60 e 100 µm**. Ulteriori riduzioni non sono consigliate perchè possono compromettere la visibilità e la resistenza meccanica.



Stent Materials:

316L Stainless Steel

- Current Designs
 - Cordis Palmaz-Shatz
 - Cordis Crossflex
 - Guidant MultiLink
 - Metronic Bestent
- Disadvantages of the Stainless Steel
 - Relatively high rates of:
 - Subacute thrombosis
 - Restenosis
 - Bleeding
 - Corrosion
 - Relatively Poor Radiopacity

316L Stainless Steel

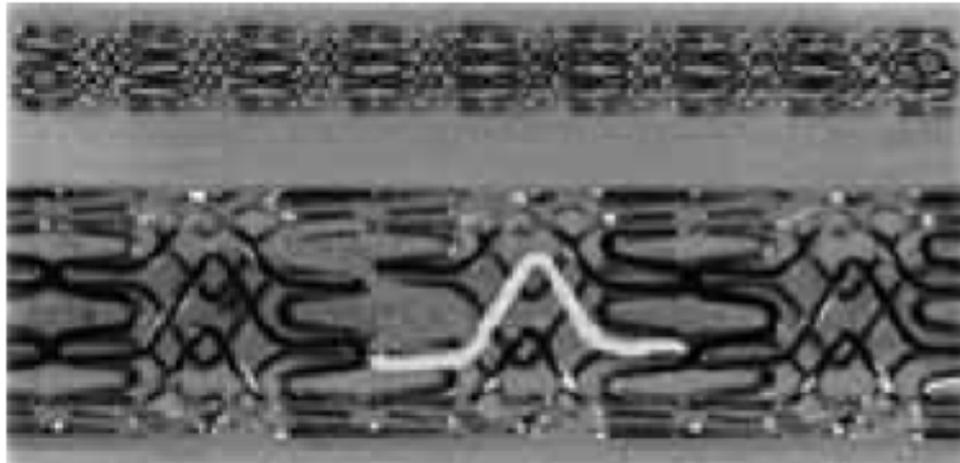
- È il materiale più usato
- Vantaggi:
 - Buona lavorabilità;
 - Emocompatibilità;
 - Basso coefficiente di ritorno elastico.



Correlation of typical yield strength values with strut thickness for a sample of devices.

Stent name/ manufacturer	Material	0.2% Yield strength (MPa)	Strut thickness (μm)
BX Velocity [®] /Johnson & Johnson	316L	340	140
Express [®] /Boston scientific	316L	340	132
Driver [®] /Medtronic	CoCr MP35N	415	91
Vision [™] /Abbott	CoCr L605	510	81

Medtronic's Bestent



Serpentine mesh

Two gold markers at the distal ends

Stent Materials:

Co-Cr-Mo Alloy (ASTM F1058 ISO 5832-7)

- First invented to make watch springs
- Current Designs:
 - Schneider Wallsten
- Proprietà migliori del 316L
 - Modulo elastico più alto;
 - Resistenza meccanica maggiore.



Stent Materials:

Tantalum

- Current Designs:
 - Medtronic's Wiktor Stent
 - Cordis Tantalum Stent
- Disadvantages :
 - More brittle than SS

Stent Materials:

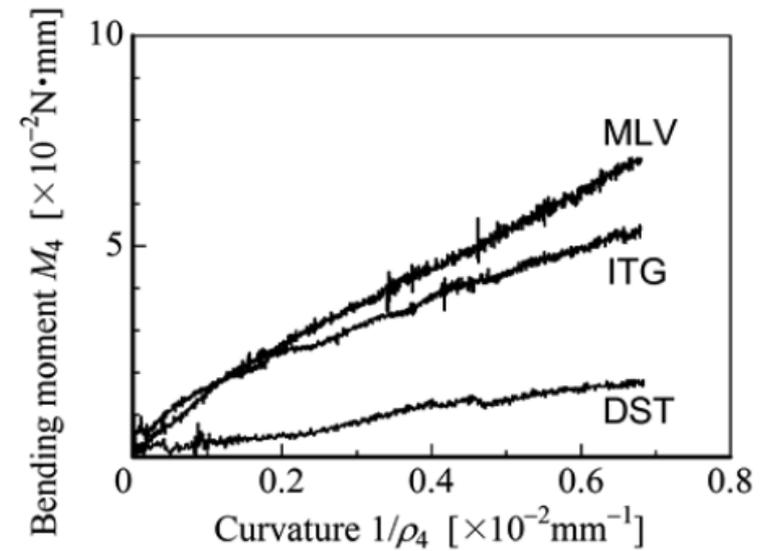
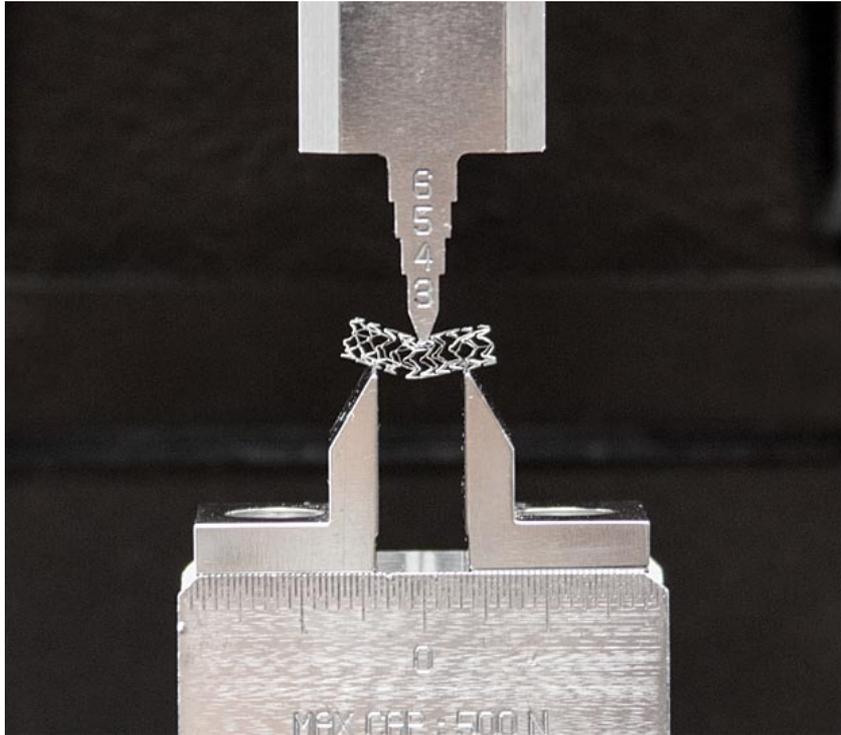
Nickel Titanium (Nitinol – NiTi)

- Super-Elastic Shape Memory
- 55% Nickel and 45% Titanium
- Ability to return to a specific shape upon heating to a certain temperature after its phase transition
- Austenitic phase vs. Martensitic phase
- Current designs:
 - Boston Scientific's Nitinol self expanding Radius
 - Boston Scientific's Symbiot stent

Stent Materials:

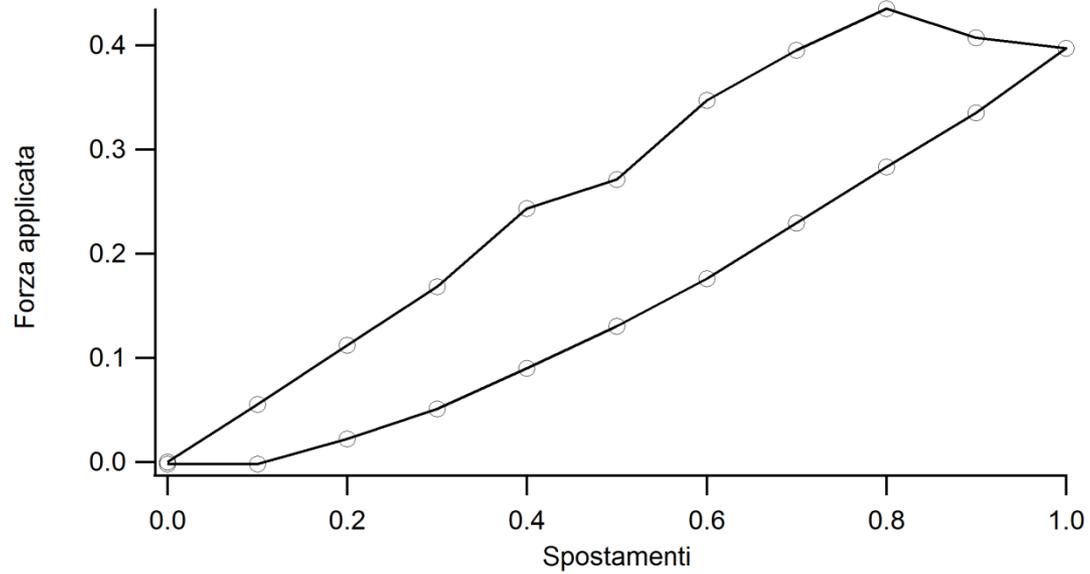
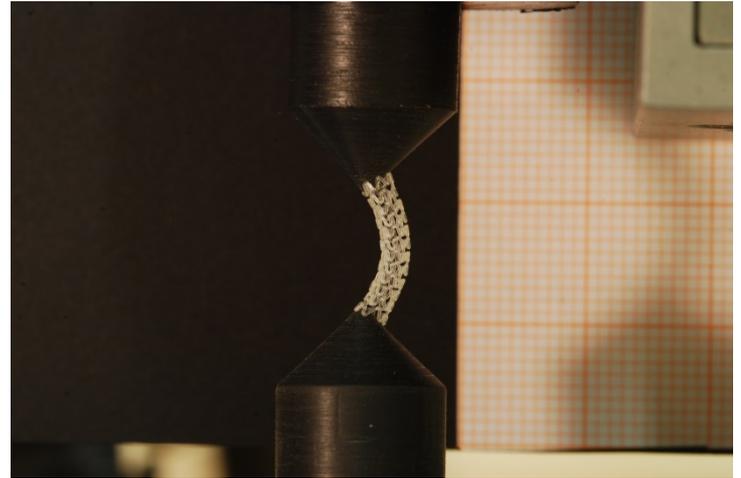
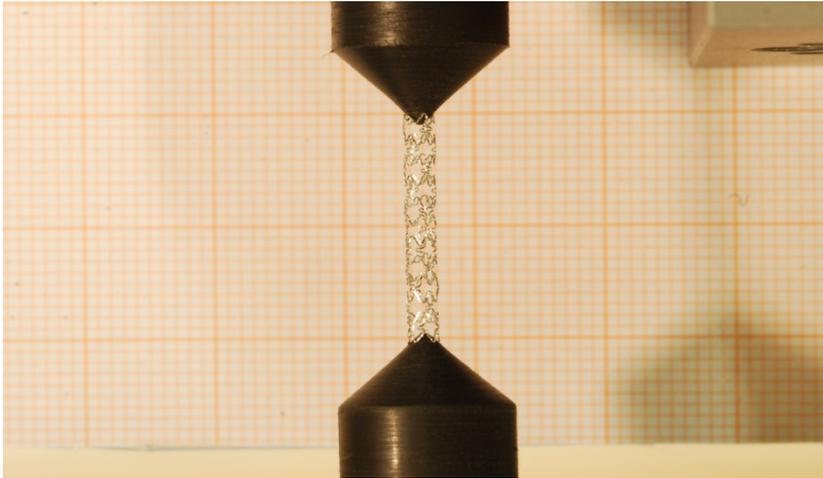
Biodegradable Polymers

- Current Designs:
 - Duke Bioabsorbable Stent
 - Collagen slotted tube
 - Cordis Biodegradable Stent
 - Blend of polylactide and trimethylene carbonate
 - CardioVasc
 - Tube paved with endothelial cells containing gel

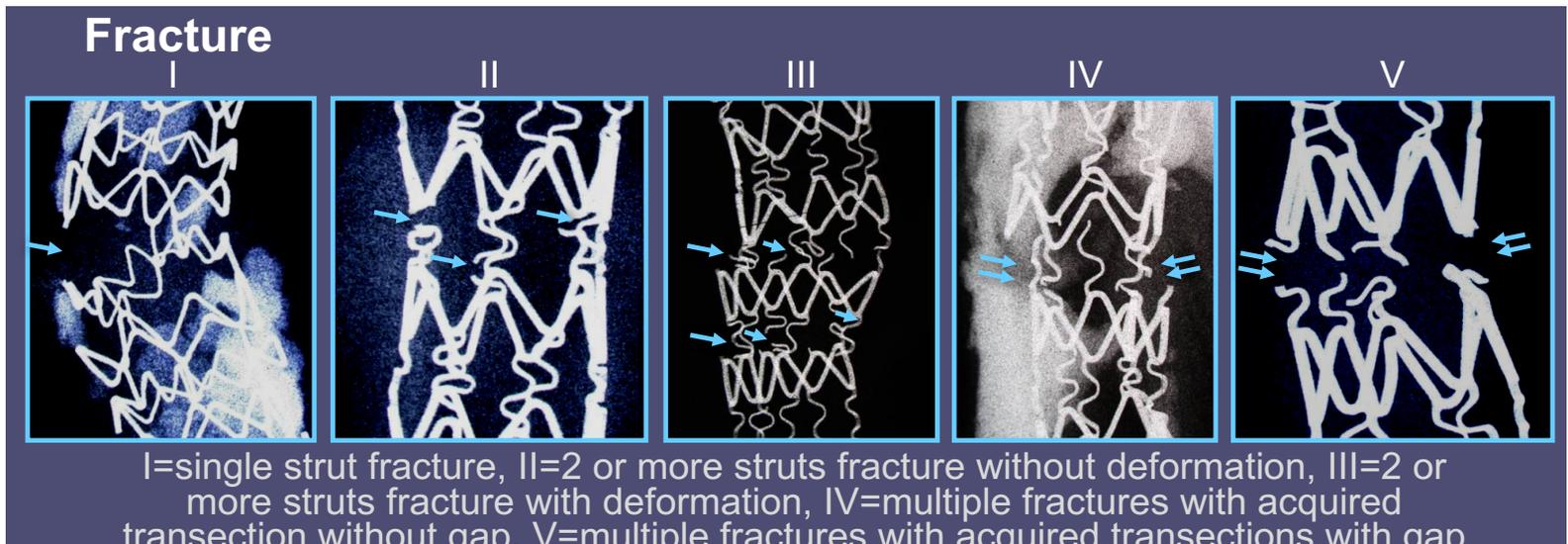


(a) Moment-curvature relation

Prove meccaniche



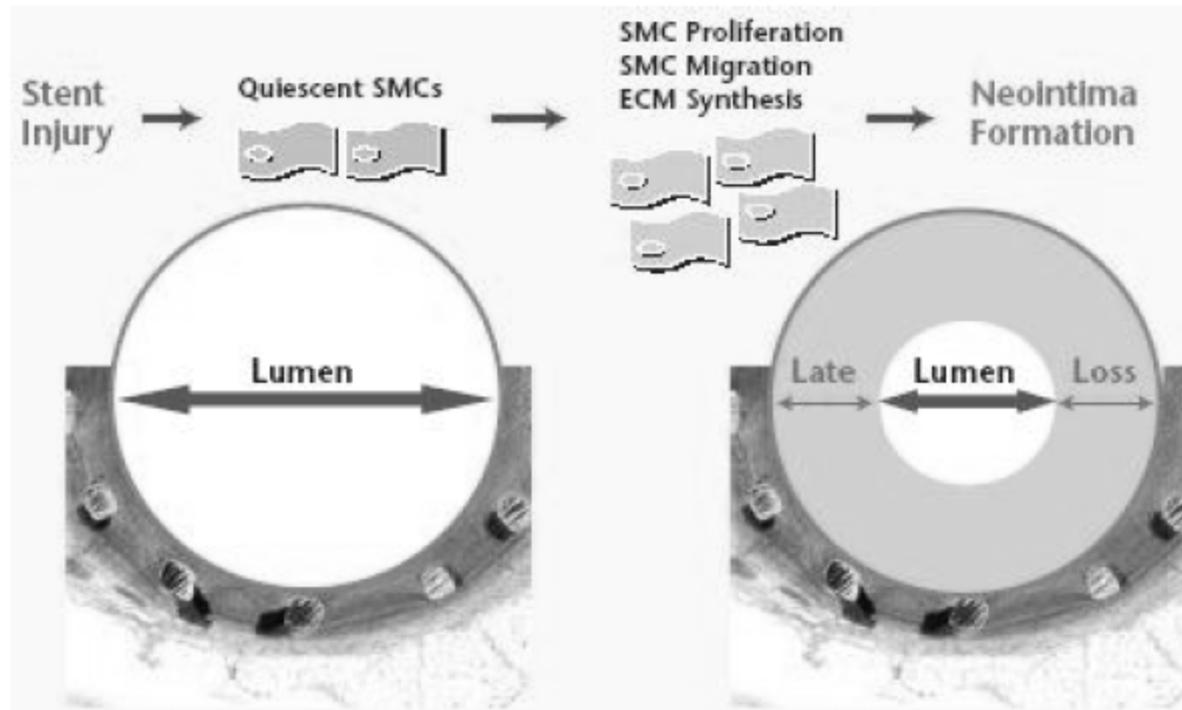
Prove meccaniche



Restenosis

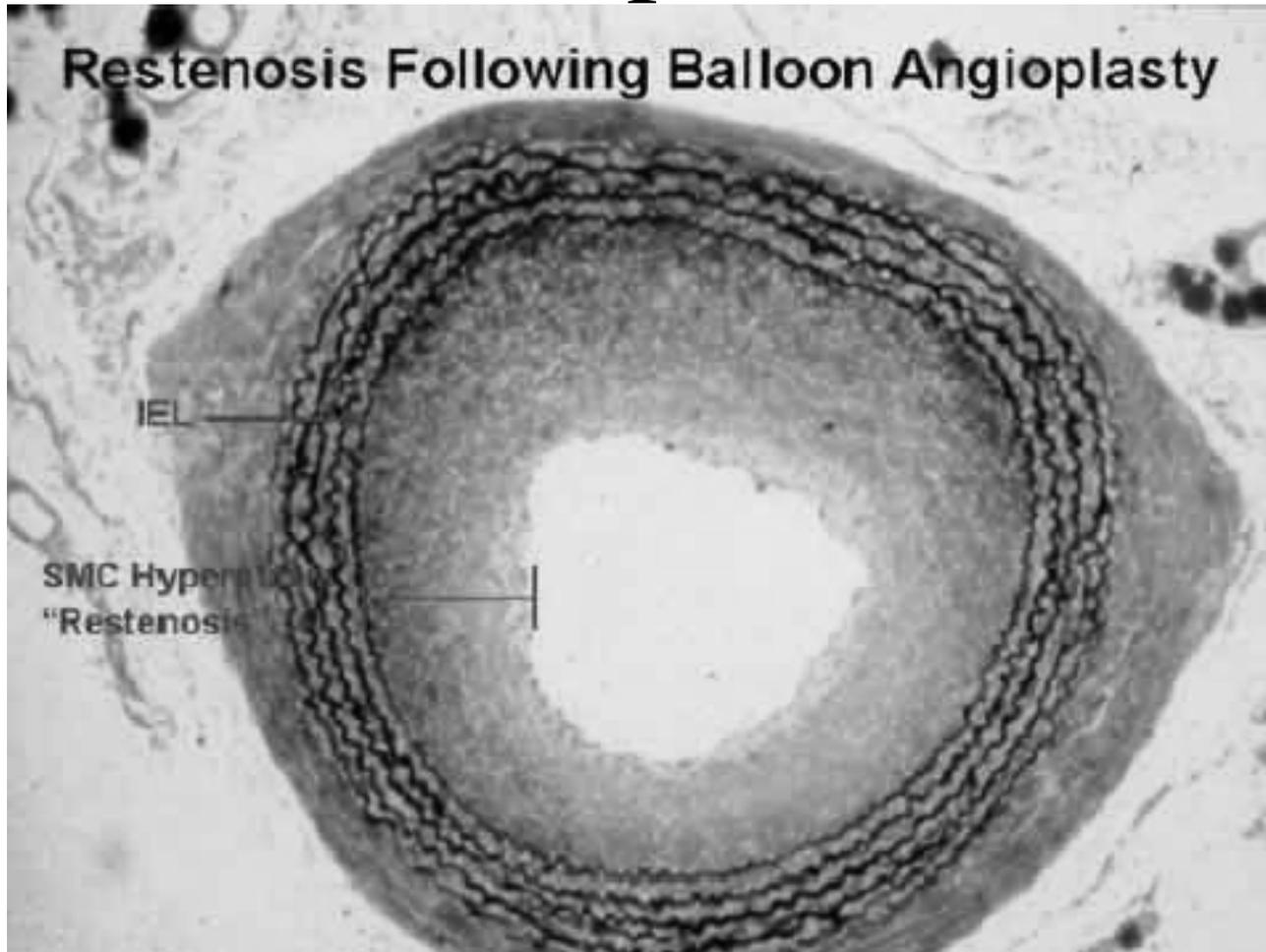
Restenosis literally means the re-occurrence of stenosis. This is usually restenosis of an artery, or other blood vessel, but possibly any hollow organ that has been "unblocked". This term is common in vascular surgery, cardiac surgery, interventional radiology, or interventional cardiology following angioplasty, all branches of medicine that frequently treat stenotic lesions.

Stent-Tissue Interaction



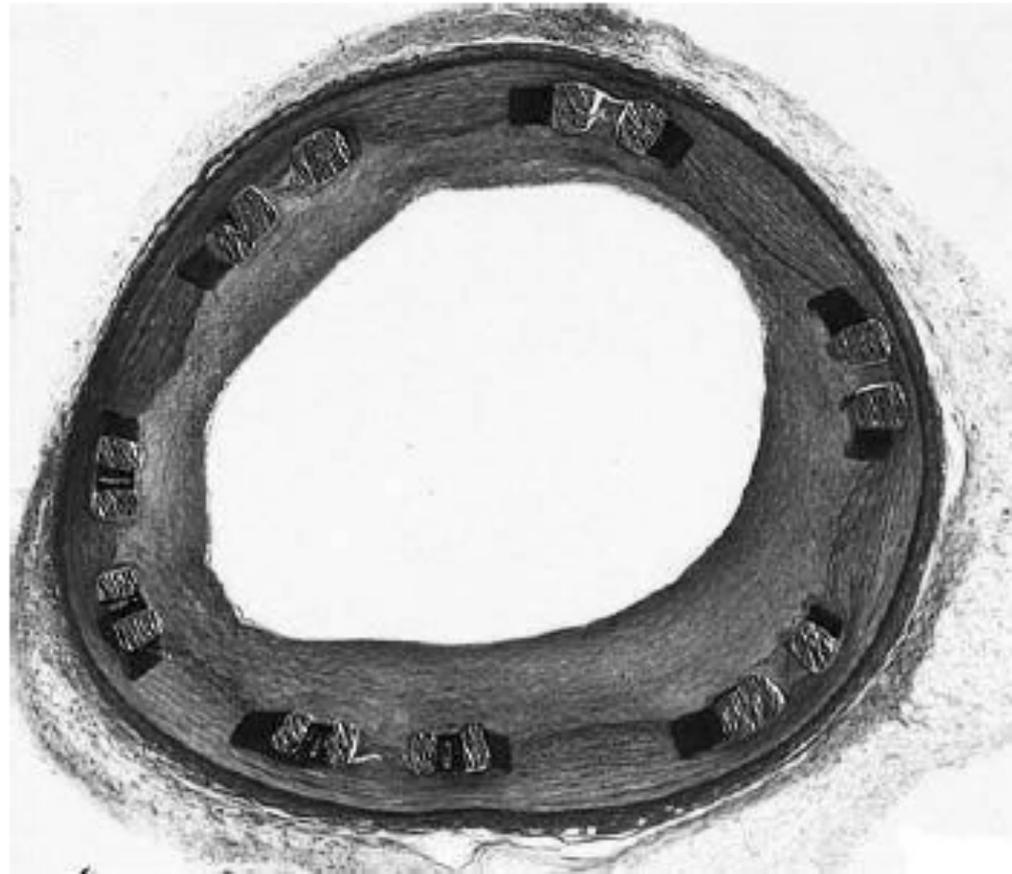
arterial smooth muscle cell (SMC)

Example (I)



Example (II)

In stent restenosis

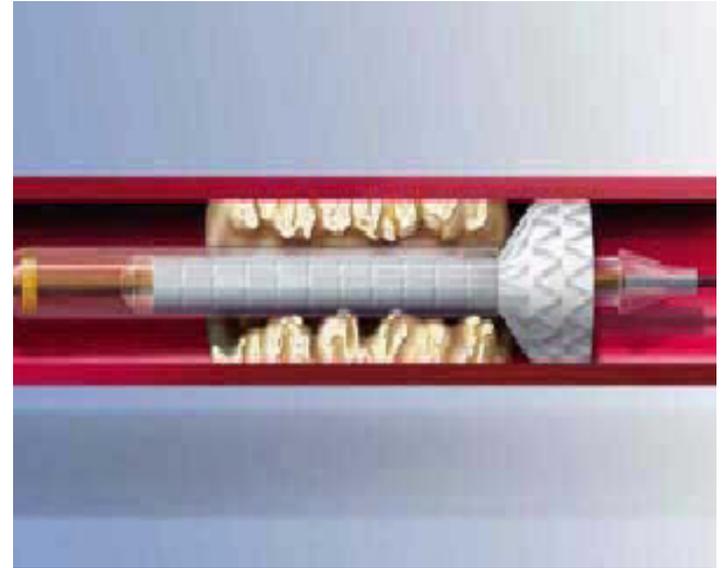


Reva medical

- **Flagship product - drug-eluting, bioresorbable stent**
- **Novel slide and lock design**
 - Tyrosine polycarbonate erodible polymeric material
 - Which acts additionally as a drug-delivery matrix
 - Licensed Rutgers Univ./ Dr. Joachim Kohn
- **Radiopaque to aid physician**

Nitinol

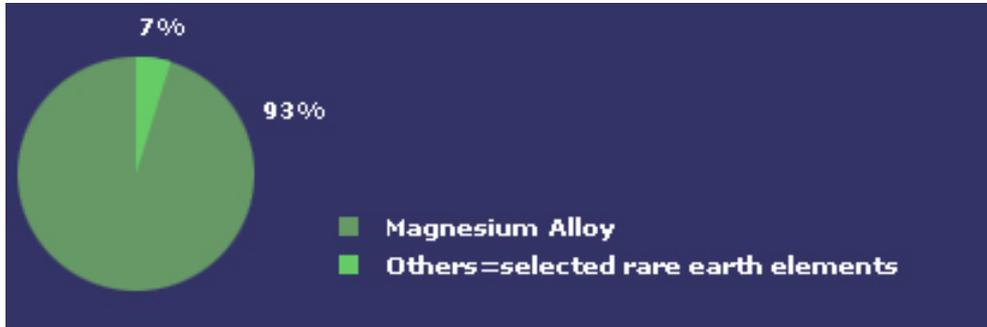
- Lega biocompatibile (55%Ni, 45%Ti);
- Presenta il fenomeno di memoria di forma;
- È superelastica.



Polimeri

- Biocompatibilità;
- Degradabilità;
- Permeabilità;
- Bassa resistenza meccanica.

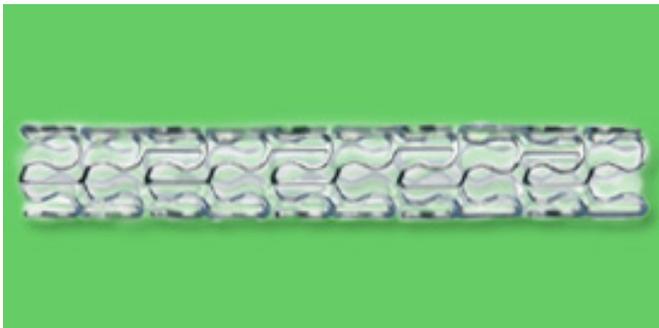
Stent al Mg (lega WE43)



Composizione:

- 93% Mg
- 7% terre rare, Zr e Y

Il Mg è alla base di una lega che combina eccellente biocompatibilità con un'ottima resistenza meccanica.



Il Magnesio: un metallo biocompatibile e bioassorbibile, la cui lavorabilità è poco nota

Il magnesio è una lega con ottime proprietà di biocompatibilità, caratterizzata da scarsa resistenza alla corrosione, che in queste applicazioni è un aspetto positivo perché a favore della bioassorbibilità. Inoltre, contrariamente alle altre leghe metalliche biocompatibili (come gli acciai inossidabili o il titanio), la corrosione del magnesio non provoca effetti tossici in quanto il magnesio è un elemento ben tollerato dal corpo umano. Per questa ragione, il magnesio è un validissimo candidato per la realizzazione di stent biocompatibili e riassorbibili in metallo.

Sostituzione dei materiali tradizionali con le leghe di magnesio pone diverse criticità che si riflettono:

- nella progettazione della mesh, intesa sia come forma che dimensione; in quanto le proprietà meccaniche del magnesio (rigidità, flessibilità, resistenza a fatica) e di resistenza alla corrosione sono molto diverse da quelle delle leghe tradizionalmente utilizzate;
- nei processi di deformazione plastica per l'ottenimento del tubo, in quanto il magnesio si lavora difficilmente per estrusione e trafilatura a freddo;
- nel taglio laser, in quanto l'interazione tra fascio termico a elevata densità, quale quello laser, e un materiale facilmente ossidabile e molto reattivo come il magnesio è poco nota;
- nei processi di finitura per asportare il danneggiamento termico e ottenere superfici a bassa rugosità, che sono poco noti nel caso del magnesio.

Microtaglio laser di stent biassorbibili in magnesio

Il taglio della mesh dello stent dal tubo precursore attualmente viene industrialmente ottenuto mediante sorgenti laser pulsate allo stato solido o in fibra attiva. Le lavorazioni pulsate, infatti, consentono di concentrare elevatissime potenze di picco in tempi molto ridotti, evitando così di caricare termicamente il componente oggetto della lavorazione; in quanto le potenze medie si mantengono limitate.

Il fuso, l'ossidazione e il danneggiamento termico nonché l'elevata irregolarità della tessitura superficiale, risultato dell'apporto termico ceduto al pezzo, vengono rimossi attraverso le successive fasi di pulizia chimica ed elettrochimica.

Lo stent viene tagliato da dei tubi di magnesio di diametro esterno 2.5 mm e di spessore 0.2 mm, che riproducono le dimensioni tipiche di uno stent coronarico prima dell'espansione.

Trattamento di rimozione degli sfridi e pulizia chimica

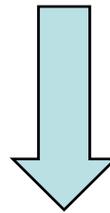
Successivamente al taglio laser, lo stent viene sottoposto al trattamento di rimozione degli sfridi e pulizia chimica. Lo stent viene pulito agli ultrasuoni in un bagno di alcool e asciugato in aria compressa. A seguito di questo trattamento, la maggior parte degli sfridi dello stent vengono eliminati.

La pulizia chimica è consistita nell'immergere per un tempo prefissato lo stent all'interno di una soluzione acida a base di acido nitrico per meno di un minuto.

Stent al Mg (lega WE43)

Proprietà:

- Facilità di introduzione
- Appropriata risposta dei vasi sanguigni
- Non trombogenicità
- Ma soprattutto...



ASSORBIMENTO FISIOLOGICO

Stent al Mg (lega WE43)

Y = 3.7-4.3%

altre terre rare 2.4-4.4%

Zr=0.4%

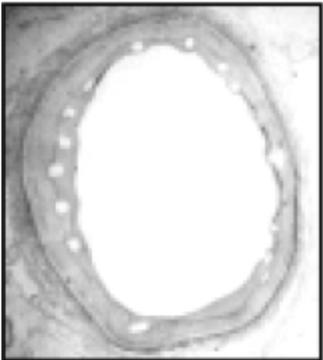
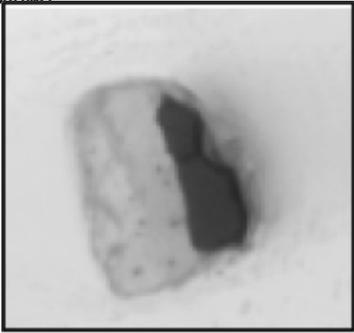
Perché stent assorbibili?

Per evitare infiammazioni croniche e danni alle pareti dei vasi sanguigni che inducono la formazione di nuove placche.

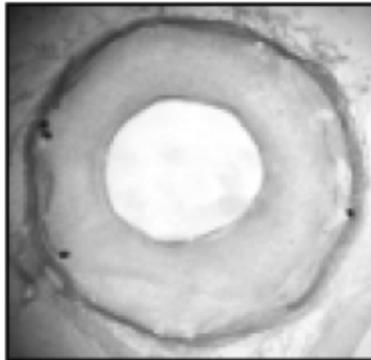
Ma dove va il Mg?

Viene assorbito dai vasi sanguigni ma i test su sangue e tessuti non hanno trovato niente di tossico. Nel nostro corpo ci sono infatti già 20g di Mg.

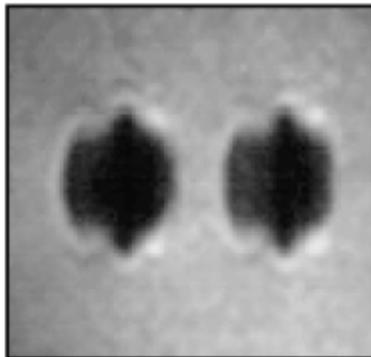
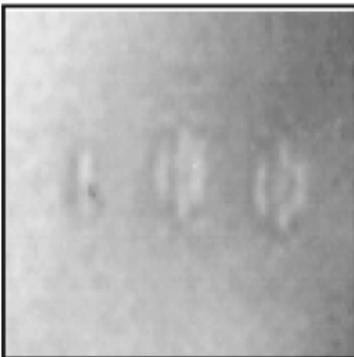
Stent al Mg (lega WE43)



Magnesium



316L



Esempio di impianto di stent di Mg in un'arteria di maiale:

Si nota che nella arteria dove è stato introdotto uno stent di Mg non sono presenti tracce di metallo.

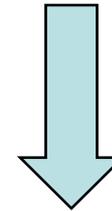
Stent al Mg (lega WE43)

Limitazioni:

✓ Radiotrasparenza



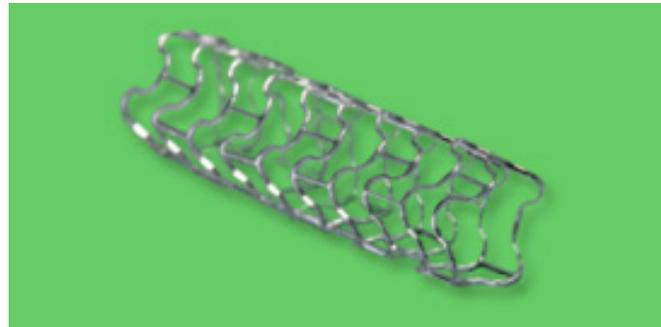
Difficoltà di rilevazione di un'embolia



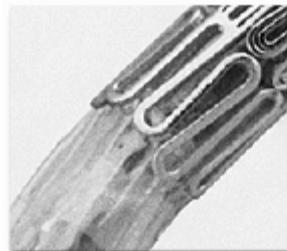
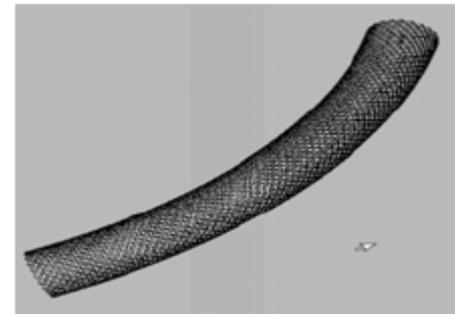
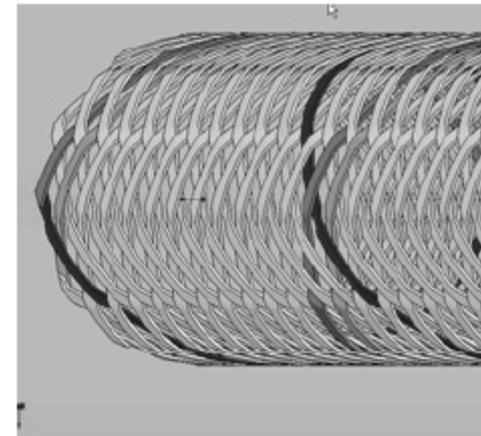
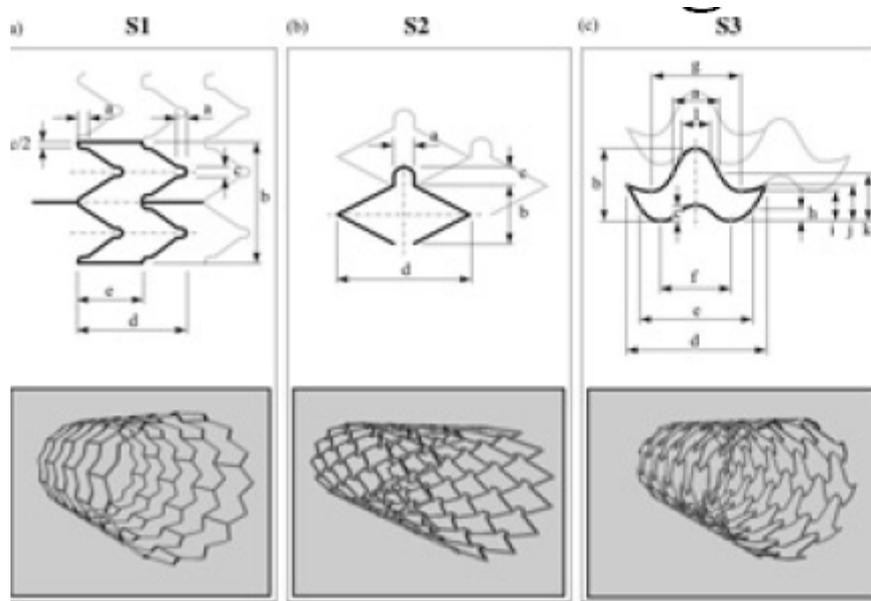
Miglioramento della visualizzazione luminosa della coronaria durante la risonanza magnetica

Conclusioni

Con stent bioassorbibili al Mg si riducono le infiammazioni che portano alla ristenosi e le proprietà da essi esibite negli studi sperimentali sono sufficienti a ridurre drasticamente la ristenosi rispetto all'uso di stent in acciaio inox.



Stent Design Parameters

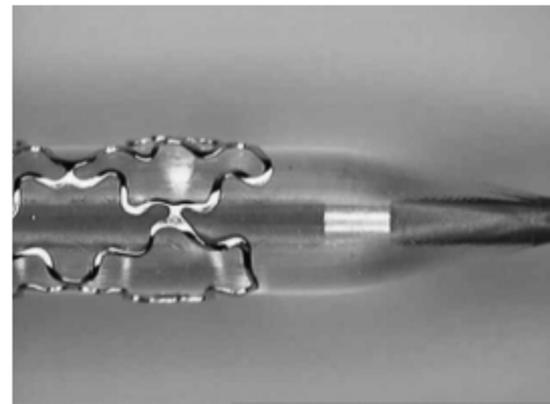
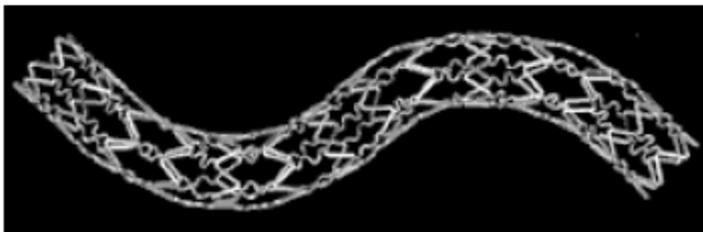
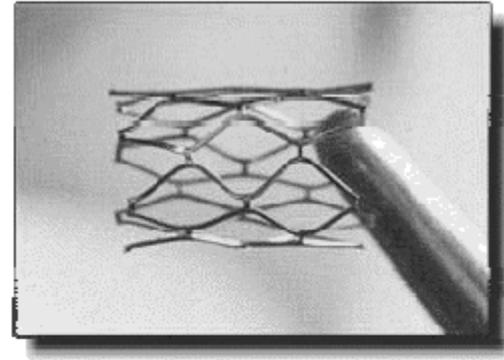
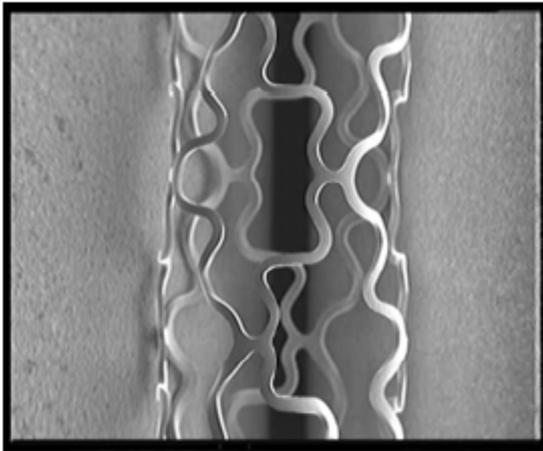


Stent Biocompatibility

- Surface area
- Thrombogenicity
- Foreign body reaction
 - Stainless steel
 - Nitinol Ni– Ti alloy
 - Plastic
- Immobilization

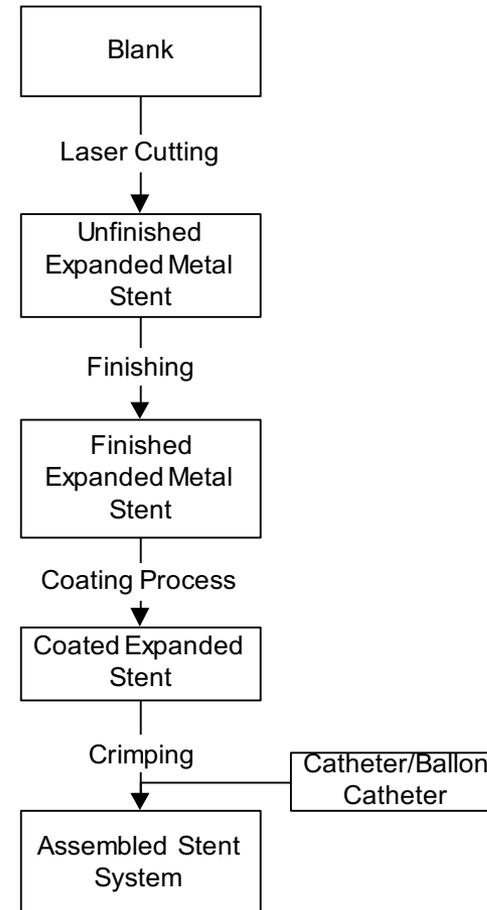
Stent design

Coiled
Laser machining



Typical Stent Production Process

- Laser cutting is a typically method for stent production
- Despite initial fabrication technique, most stents see a similar fabrication process



Laser Cutting

- Allows precise cutting of stent designs from tubular blank
- Computer Controlled mechanism allows for flexibility in stent designs



Stent Finishing

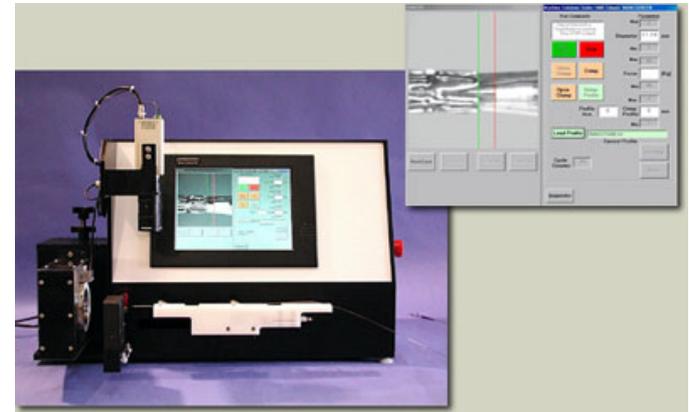
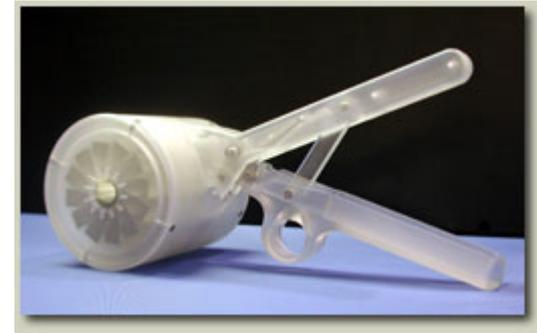
- Precision laser cutting can leave unfinished edges on the stent.
- Stents are finished in various ways:
 - Laser Deburring/Chemical Finishing
 - Electropolishing/Electroplating
- Finishing method is dictated by the desired surface of the stent; Especially if further coating is added.

Coating

- Since the coating is critical to stent functionality, it drives many decisions about stent production.
- Coating procedure is dictated by the material being coated. Options include: spraying and dipping.

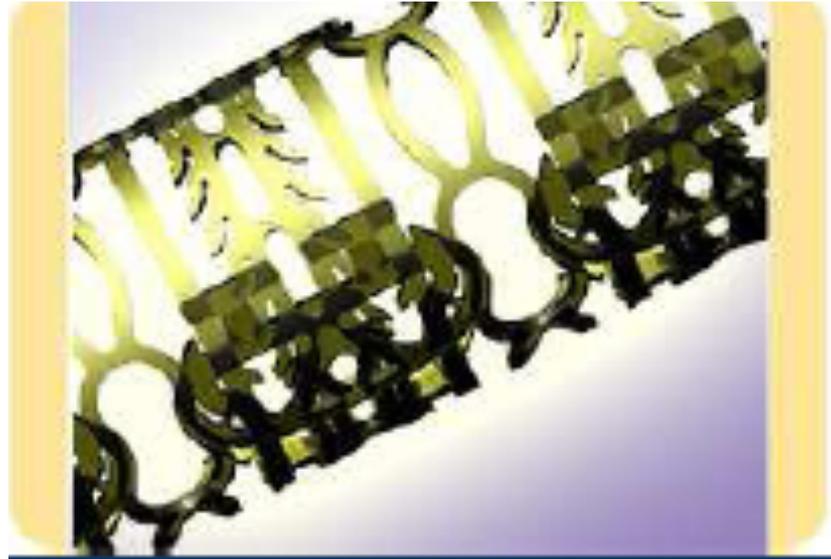
Crimping

- Stents are typically produced in their expanded form.
- Crimping collapses the stent onto its associated hardware.
- Crimping can be done by the manufacturer or prior to catheterization in the clinic.



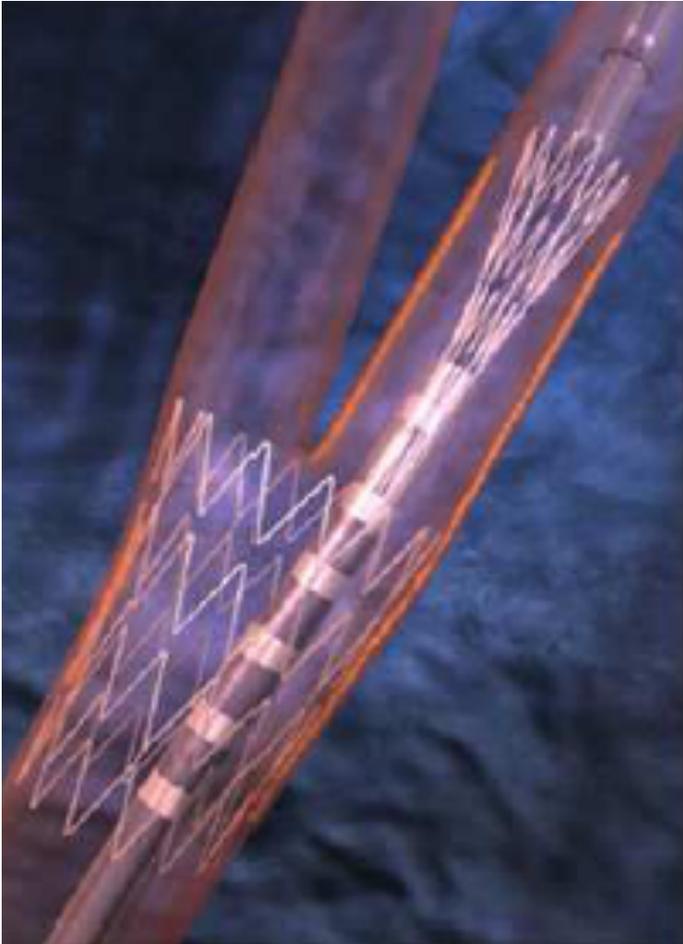
Alternate Stent Production Methods

- Metal Injection Moulding
- Assembly from Wire

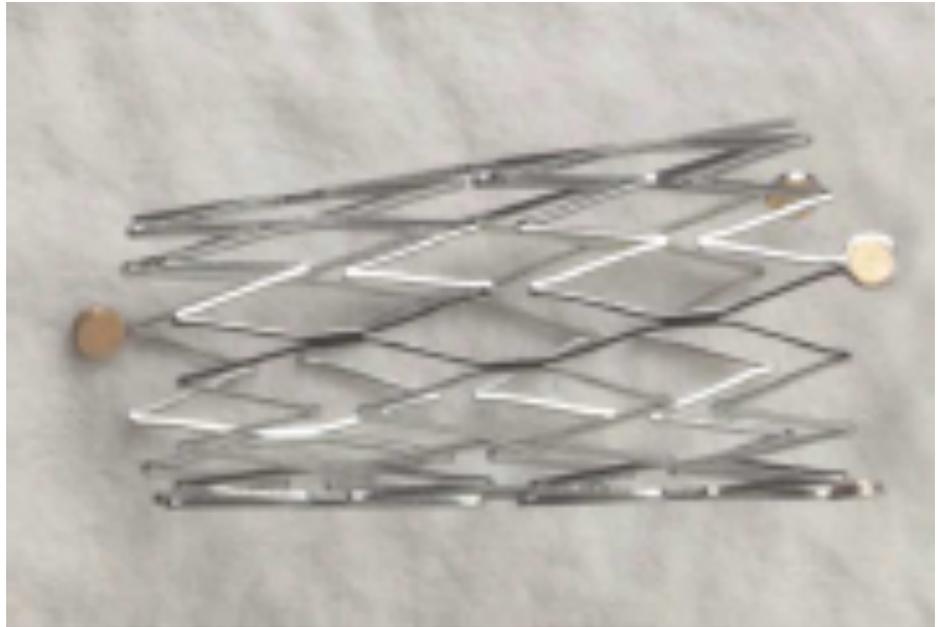


Devax, inc.

- **Flagship product – drug-releasing (biolimus A9) bifurcation stent**
 - Nickel/titanium alloy, conical shape
- **Allows placement of stent in side branch**
- **Clinical Trials**
 - Does not obstruct flow to side vessel
 - Low restenosis rate $< 8\%$



15/12/20



Stent destinations of use (I)

Cardiovascular (heart) stents

Materials: Stainless Steel, Ti,
Cobalt Chromium

Wall thickness: 0.08-0.40mm

Outside
diameter:
from 0.80 to
2.0mm



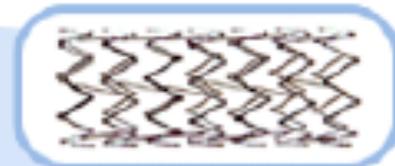
Stent destinations of use (II)

Peripheral (throat, intestine) stents

Materials: Nickel Titanium (nitinol) for maximum elasticity

Wall thickness: 0.05-0.30mm

Outside diameter:
from 4 to
15mm



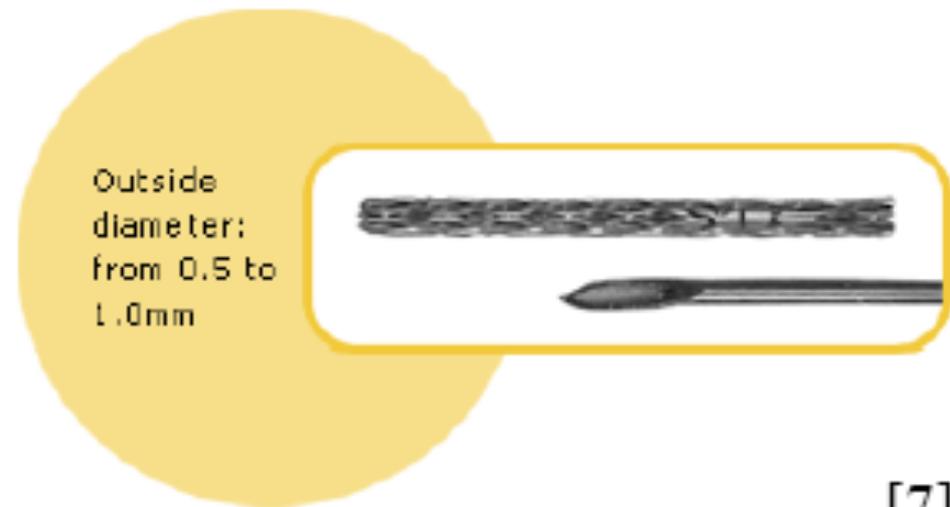
Stent destinations of use (III)

Brain (blood vessel) stents

Materials: Stainless Steel, nitinol, Platinum, Titanium, Cobalt Chromium

Wall thickness: 0.05-0.10mm

Human hair is about 0.1mm thick

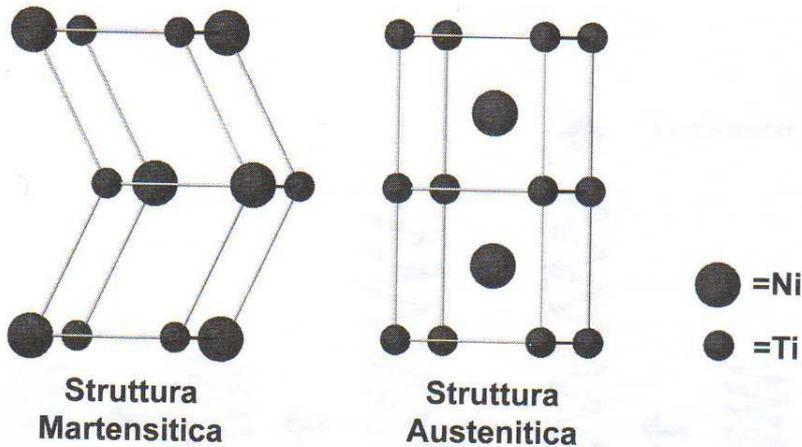


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STENT - NITINOL

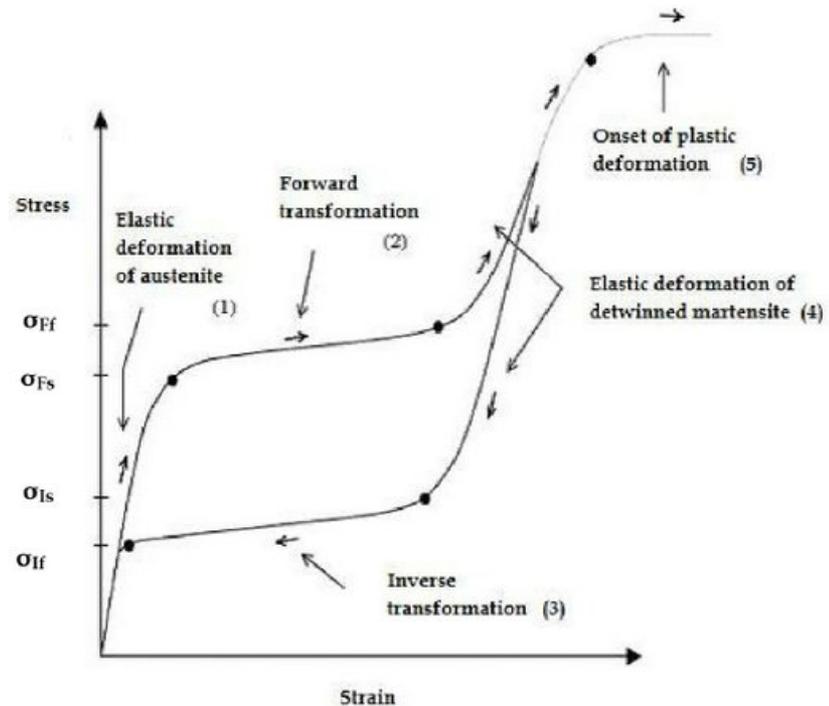
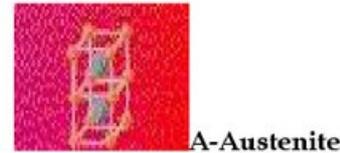


Shape Memory Alloy uses



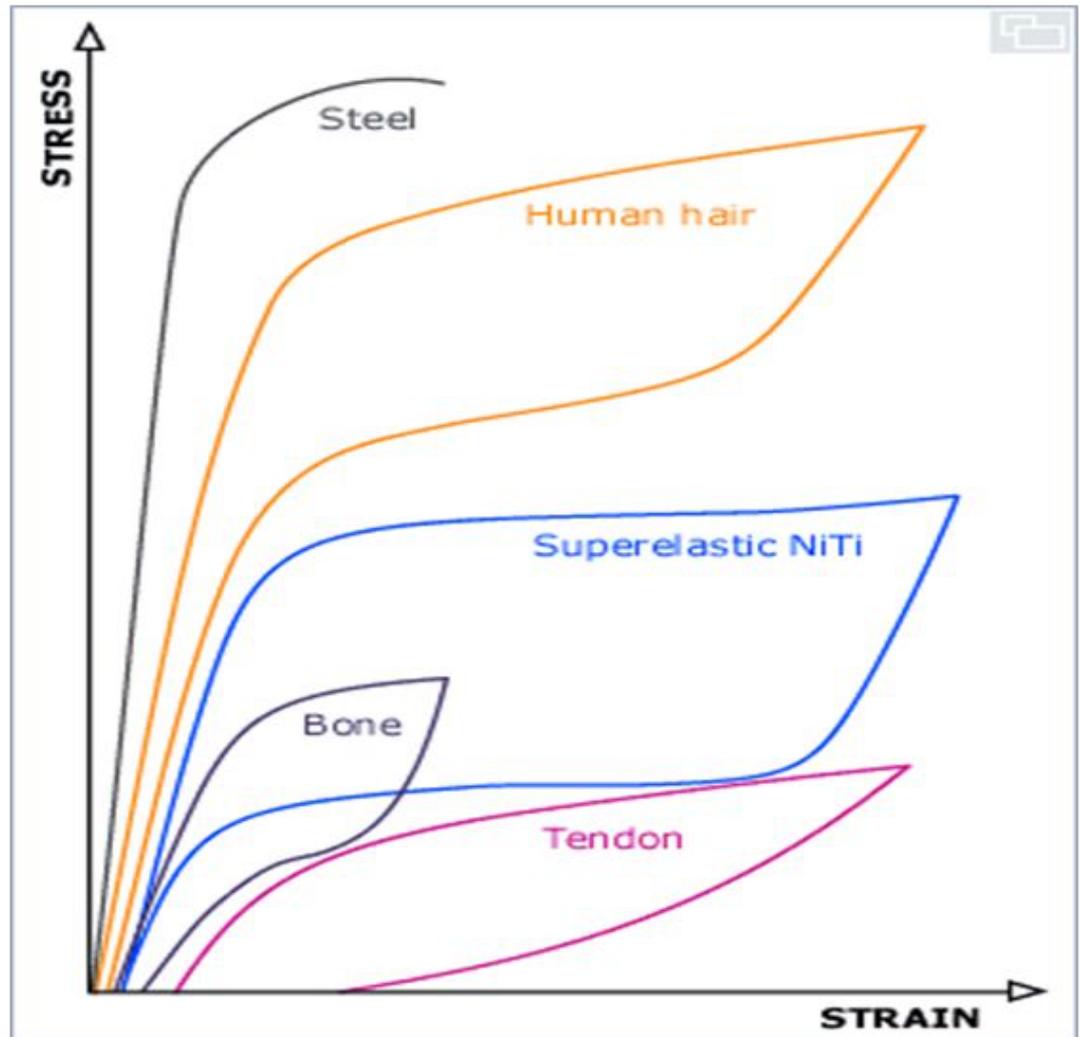
Struttura cristallina Nitinol

- Struttura austenitica: reticolo cubico a corpo centrato
- Struttura martensitica: reticolo monoclinico ortorombico

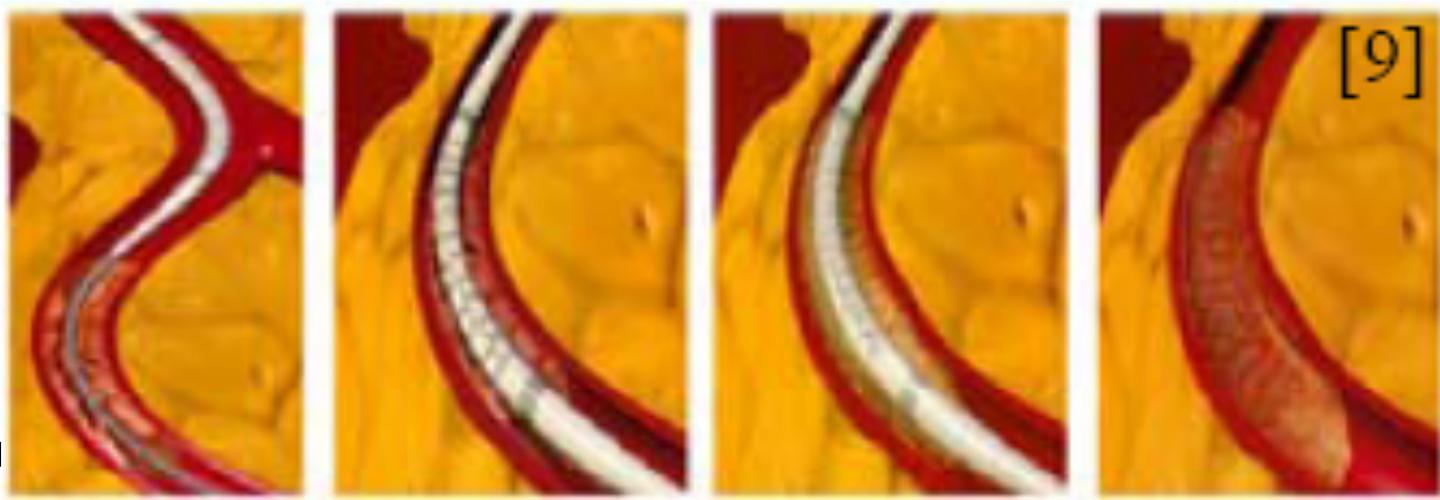
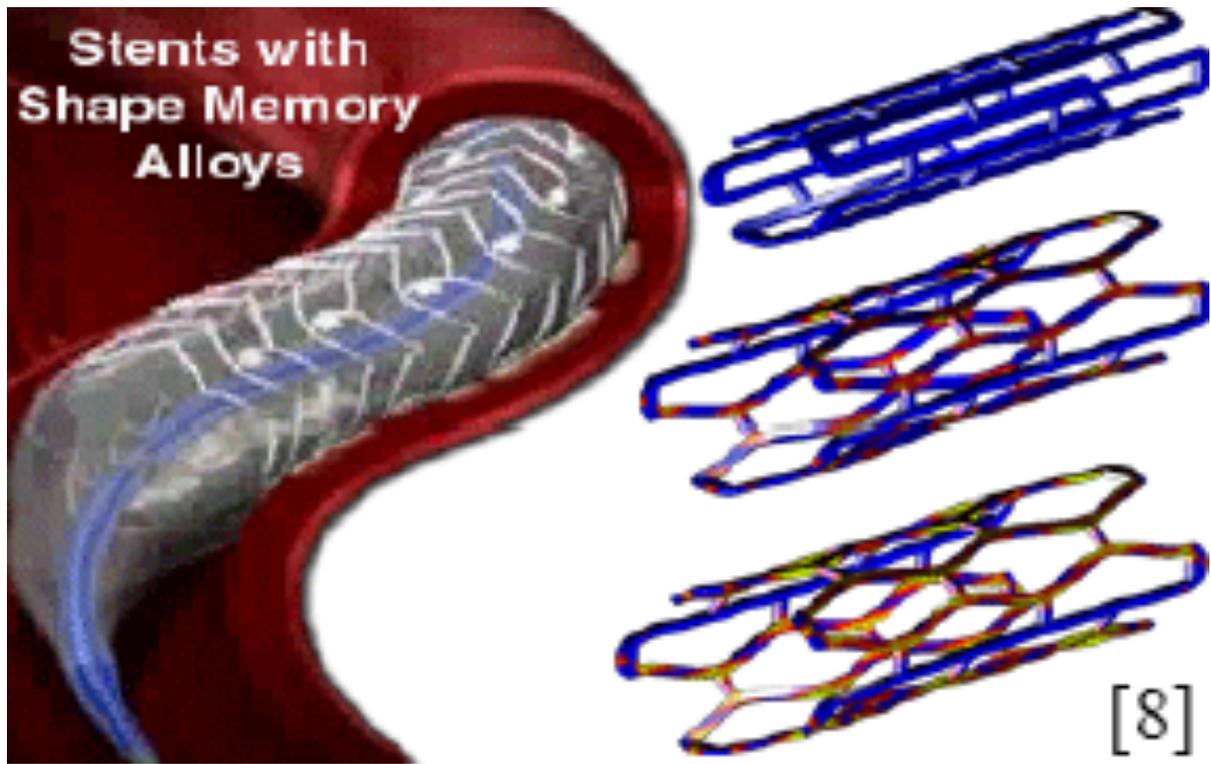


Example of Biomedical Application:

The Superelasticity of NiTiNol appears to be much more physiologic compared to stainless steel, for example.

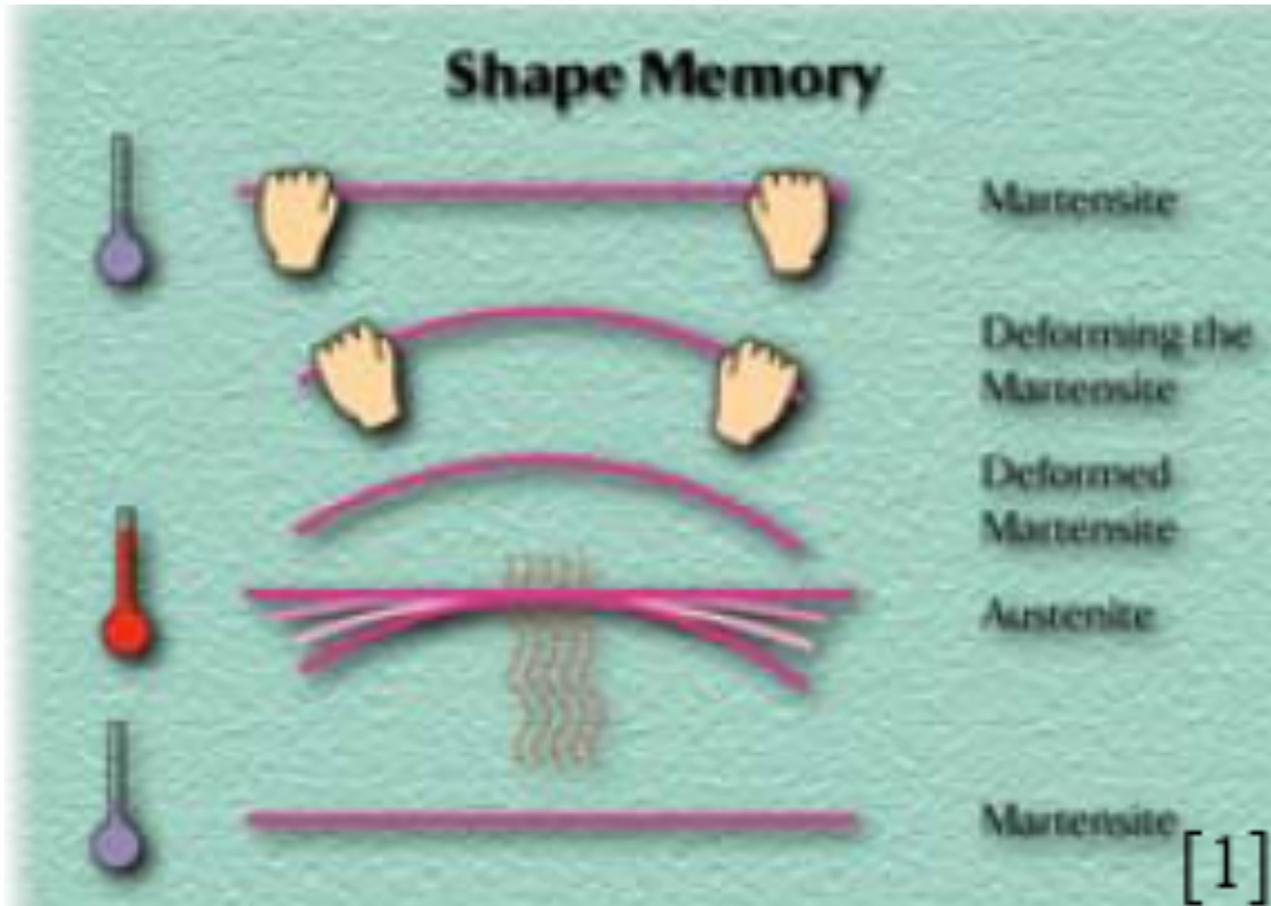


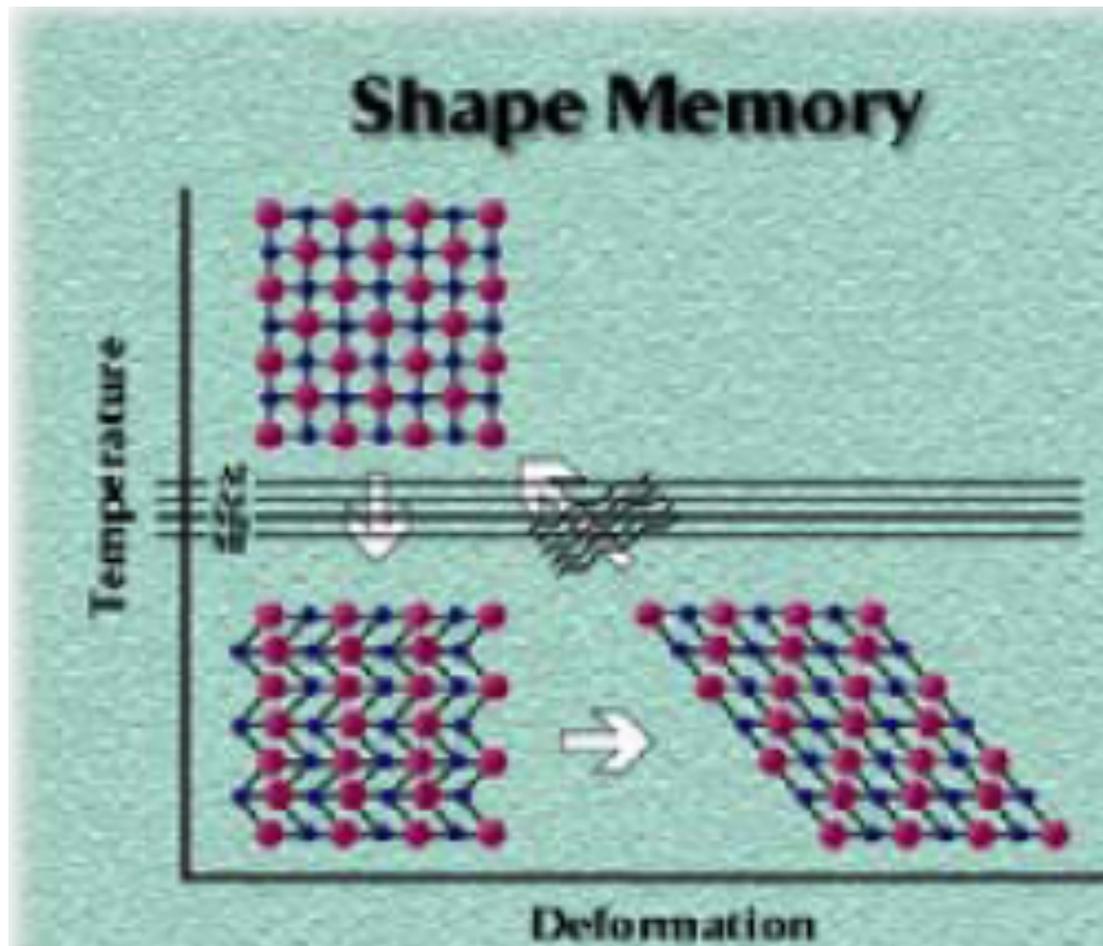
- A stent is used to open up, and hold open, a **constricted pathway** in the body.
- Shape memory alloy stents **apply pressure** to the tube wall, giving enhanced support to the pathway.

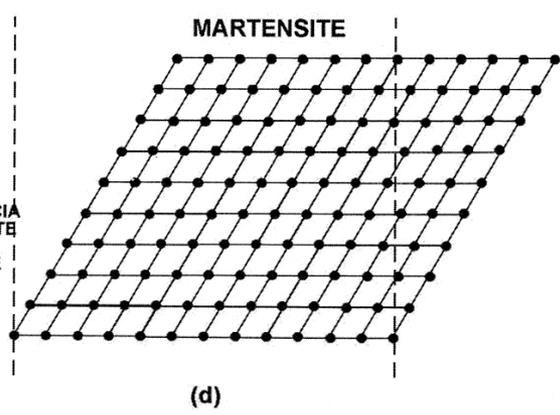
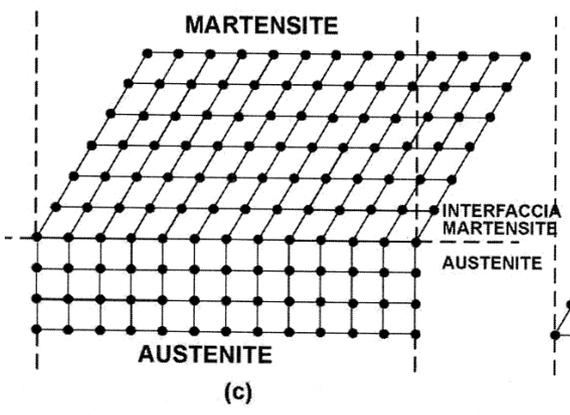
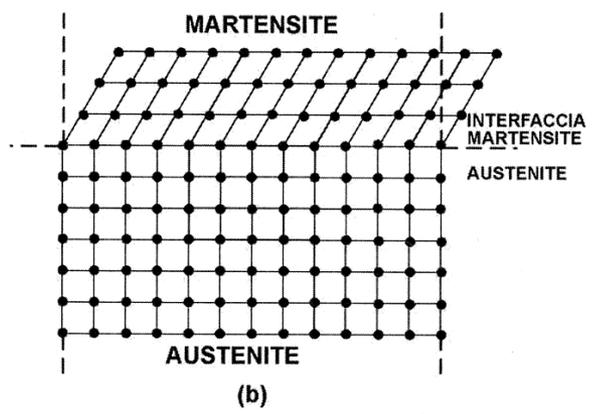
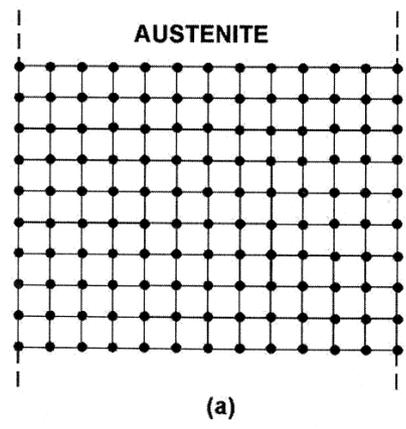


What is a SMA?

- An **alloy** is a mixture of two or more pure metals, such as Nickel and Titanium, known as NiTi or Nitinol
- The **Shape Memory Effect** is the ability of some materials to bend, stay bent, then after some signal, return to its original shape.
- Shape memory alloys use **atomic rearrangement** to “remember” their original shape.
- Special symmetry in the atomic arrangement, called “**twins**” allows the material to change shape easily, and change back after given a signal.







BASSE TEMPERATURE

