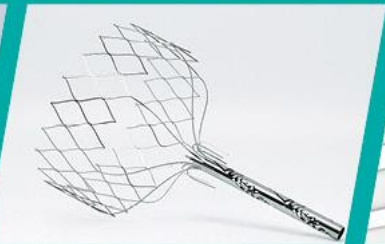
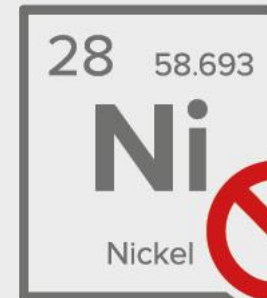


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MEDTECH

Developing Nickel-free Implants for Allergic Patients



PRECISION IS OUR PROFESSION

[_Meko.de](https://www.meko.de)

MeKo
MEDTECH

Agenda

MeKo MedTech

Vasculoy[®] - Ni-free Alloy for Permanent Stents

Questions & Answers

Where the story begins



In May 1991, Clemens Meyer-Kobbe started MeKo as a one-man business.

MeKo Manufacturing e.K.



2026*

1997

2000

2007

2022

2023

MeKo Manufacturing e.K.

Laser material
processing and post
processing

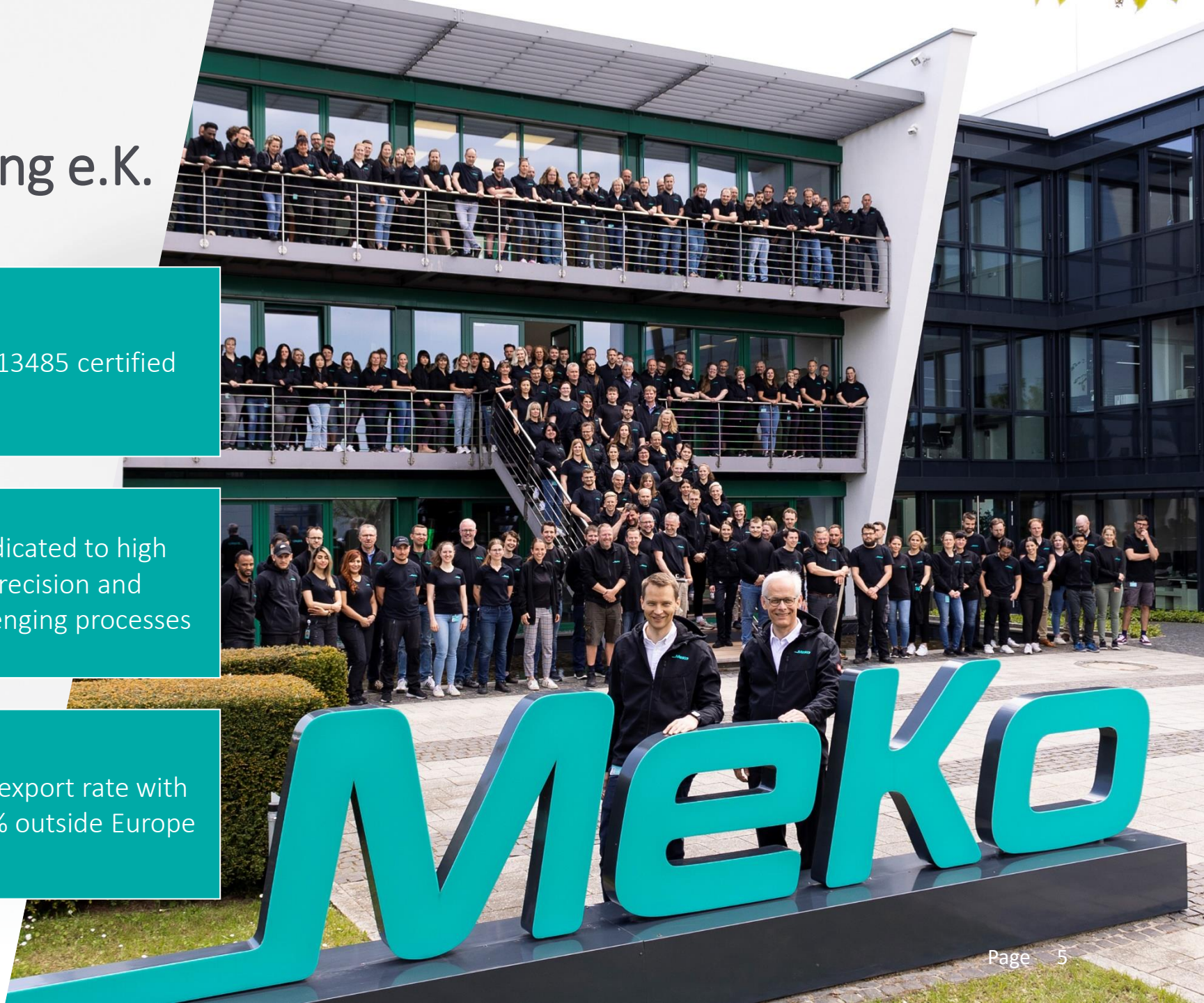
ISO 13485 certified

More than 300 qualified
employees

Dedicated to high
precision and
challenging processes

Development of new
materials, optimizing of
material properties

High export rate with
> 50 % outside Europe



Huge Stock for Rapid Prototyping

- More than 3.000 different tube and sheet lots on stock
- Available materials:
 - > 316L medical, L605, Phynox, MP35N
 - > NiTi (Nitinol)
 - > Bioresorbables:
Mg / Resoloy[®], Fe, Zn, polymers / PolymediX[®]
 - > Vasculoy[®] (Nickel-free alloy)
- Securing material quality thanks to in-house inspection and measuring instruments for material properties

Manufacturing Processes for Medical Devices



Laser Cutting / Drilling

- Nearly no limitations in cutting length and tube diameter
- Superior dimensional accuracy

Laser Welding

- Spot welding and seam welding
- In-process quality control

Heat Treatment / Shape Setting

- Extremely fine grain sizes
- Controlled heating cycles ensure reliable Af-temperature setting

Electropolishing

- Widely adjustable range of material removal

Passivation and Final Cleaning

- Automated passivation / cleaning line for consistent results
- Enhanced biocompatibility

Quality Inspection

- 100 % inspection of all implants
- Visual and automatic microscopes

Research and Development

- Production technologies for resorbable implants
 - > **PolyMediX**[®], high-precision polymer tubes with drug integration in the tube wall
 - > **Resoloy**[®], the new magnesium alloy
- The alternative to the elaborated stent materials
 - > **Vasculoy**[®], the nickel and cobalt free material for stents

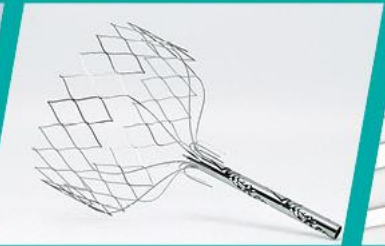
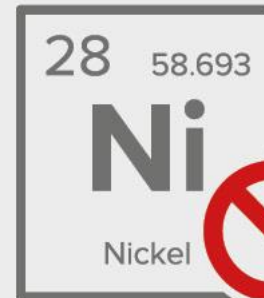
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Vasculoy®

The new and only Ni-free alloy
for permanent stents



Agenda

- ① Why a Ni-free Alloy?
- ② Material Requirements for Stents
- ③ Vasculoy[®] - The New Material?
- ④ Material Properties of Vasculoy[®]
- ⑤ Vasculoy[®] in comparison
- ⑥ Road Map of a Vasculoy[®] Stent

Why a Ni-free Alloy?

① Allergy

- Studies show that approximately **13 %** of the population are allergic to nickel with a strong upward trend [1].
- Individuals, who are allergic to nickel, demonstrate a greater **restenosis** rate [2, 3].
- Furthermore, the corrosion products of 316L are toxic to the primary culture of vascular smooth muscle **cells** when the nickel concentration is higher than 11.7 ppm [4].



Why a Ni-free Alloy?

① Allergy

Patients with a severe Ni-allergy are seldom but show immediately significant symptoms.

Two samples are shown in the next slides.



Why a Ni-free Alloy?

① Allergy



Pruritic and an eczematous dermatitis worse on the right leg after NiTi stent implantation [5]



Resolution of dermatitis one month following stent explantation [5]

Why a Ni-free Alloy?

① Allergy



Location of iliac stent (arrow) [6]



A picture on admission showing rash around abdomen [6]

After iliac stent explantation:

“Postoperatively, her dermatitis significantly improved, and her depression disappeared immediately.” [6]

Why a Ni-free Alloy?

① Regulatory Requirements

- The European Parliament and Council passed the Nickel Directive:
 - > limits **nickel content** in products used for epithelization after piercing to 0,5 ‰ mass of Ni to total mass [7]
 - > limits **nickel release** from objects intended for use in direct and prolonged contact with skin to 0,5 µg/cm² per week [7]
- The FDA released two information regarding implants with Ni-content:
 - Biological Responses to Metal Implants [8]
 - Guidance for Industry and Food and Drug Administration Staff:
“Corrosion of implant devices made of, or having components made of, nickel-rich alloys (e.g., nitinol, stainless steel, MP35N) results in the release of nickel ions, which may lead to various modes of toxicities.” [9]

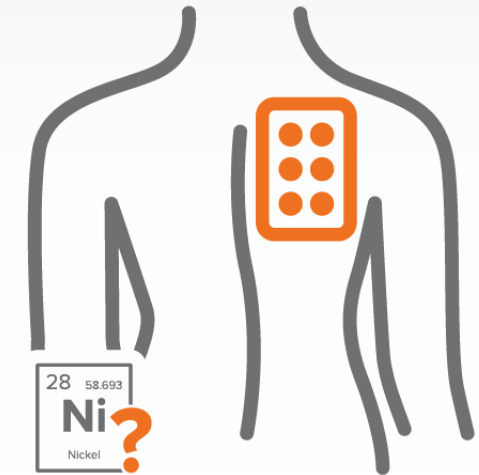
Why a Ni-free Alloy?

① Responsibility and Liability

Who takes the **responsibility** for implanting a nickel-containing device if an identical Ni-free device is available?

Can Ni-allergic patients claim for **indemnification** if they experience restenosis?

Patients must be **tested for Ni-allergy** before implantation of a Ni-containing implant.



Patch Test!

② Material Requirements for Stents

Material properties

- Mechanical properties
 - Strength _____
 - Strain / Plasticity _____
- Corrosion resistance _____
- Biocompatibility _____
- MRI compatibility _____
- Radiopacity _____

Requirements

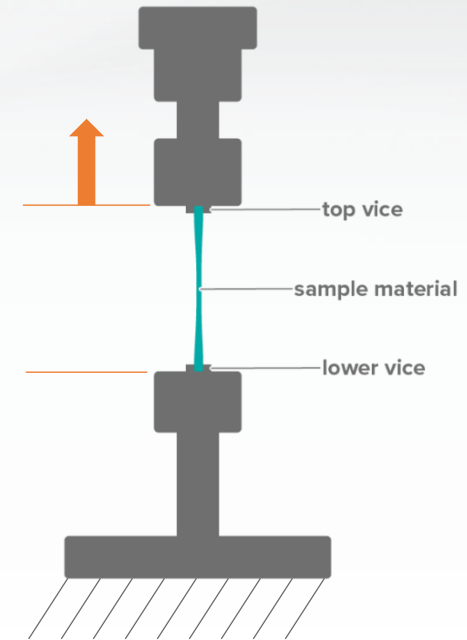
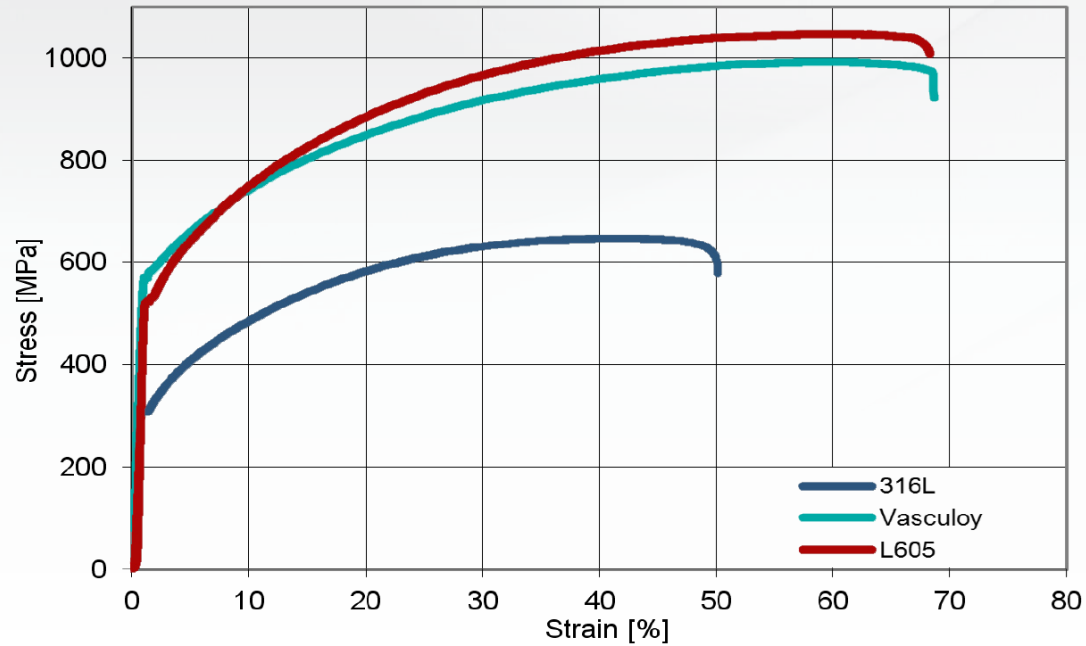
- Thin strut sizes
- Highly deformable without cracks
- No degradation or ion releases
- No negative tissue reactions, **Ni-free**
- No artifacts under MRI
- Angiographic visibility under X-ray

③ Vasculoy® - The New Material?

- There are many Ni-free industrial alloys:
all have a high strength but **no** plasticity → not suitable for stents
- A special alloy for vascular applications was developed by MeKo:
 - Based on stainless steel but **Nickel is replaced by Nitrogen**
 - > nitrogen stabilizes the austenite grain structure
 - > with the nitrogen content in the alloy the material properties are adjusted for stents

A teal-bordered box containing the text "Vasculoy® by MeKo" in teal, followed by an equals sign and "Vascular Alloy" in teal. The "Vasculoy" is in a bold, italicized font, and "by MeKo" is in a smaller, sans-serif font.

Strength and Strain



Vasculoy®

- High strength and break elongation
- Nearly identical to L605

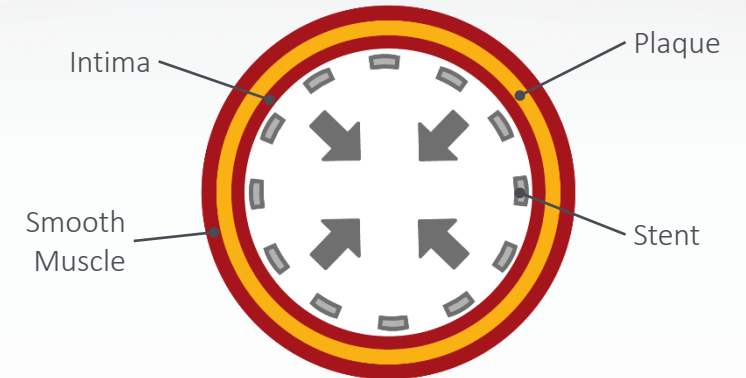
Material Properties of Vasculoy®

4 Recoil



Tests performed according to ISO 25539-2 and ASTM F 2079

Stent Location	316L			Vasculoy®			CoCr - L605		
	Distal	Middle	Proximal	Distal	Middle	Proximal	Distal	Middle	Proximal
Diameter _{inflated} in mm	3,87	3,87	3,88	3,76	3,8	3,87	3,79	3,79	3,83
Diameter _{final} in mm	3,72	3,72	3,75	3,56	3,6	3,63	3,58	3,58	3,6
Stent Recoil in %	4,0	3,5	3,5	5,5	5,5	6,0	5,5	5,5	6,0



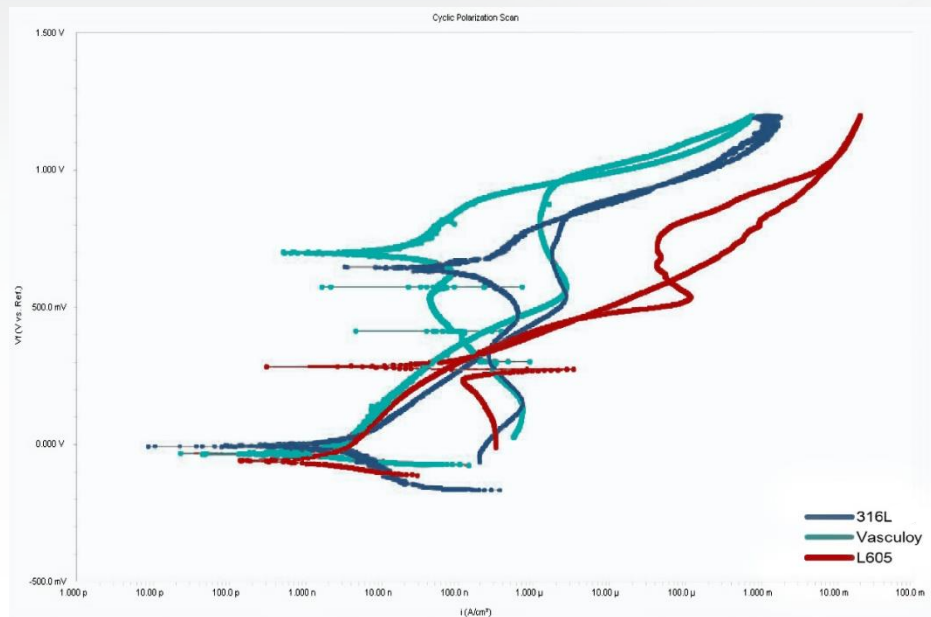
- Recoil equivalent to L605

Material Properties of Vasculoy®

4

Corrosion Resistance

Cyclic potentiodynamic analysis according to ASTM F2129 is used to study the corrosion behavior of metallic materials



	316L	Vasculoy®	CoCr - L605
Protection Potential E_p in mV	859	1040	591
Breakdown Potential E_b in mV	823	842	769
Passive range in mV	825	1058	802

Vasculoy®

- Best corrosion resistance of all stent materials

4 Material Properties of Vasculoy® Biocompatibility

Biocompatibility investigations according to EN ISO 10993

	Vasculoy®
Cytotoxicity test (EN ISO 10993-5)	No proliferation inhibition
Hemolysis elution method (EN ISO 10993-4)	No hemolytic effects
Hemocompatibility dynamic conditions (EN ISO 10993-1)	No activation of the coagulation system
Chemical analysis quantification of inorganic leachable substances (EN ISO 10993-1)	No quantifiable leachable substances
Chemical analysis detection of organic substances (EN ISO 10993-12)	No detectable substances



Vasculoy®

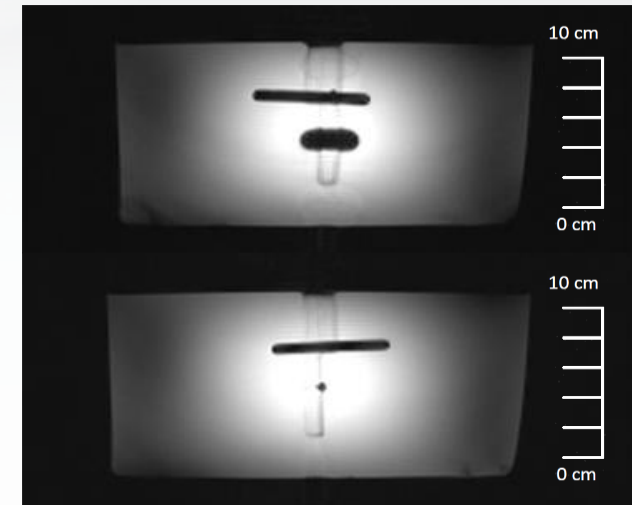
- Perfect biocompatibility
- No compromises

4

Material Properties of Vasculoy® MRI Compatibility

Tests were performed according to the standard test method ASTM F2052, ASTM F2119 and ASTM F2182

	316L	Vasculoy®	CoCr – L605
Magnetically Displacement Force 3 Tesla			
Weight of Probe in $N \times 10^{-4}$	2,65	2,88	2,79
Displacement Force in $N \times 10^{-4}$	0,6	0,3	0,24
Force resulting deflection angle in °	13	7	5
Radio Frequency Induced Heating 1,5 Tesla			
Probe / Reference Probe in °C	0,8 / 0,9	0,7 / 0,8	1,3 / 1,1
MR Image Artifacts 1,5 Tesla			
Spin / Gradient echo artifact in mm	4,7 / 6,4	2,6 / 5,5	3,4 / 4,6
MR Image Artifacts 3,0 Tesla			
Spin / Gradient echo artifact in mm	5,5 / 8,2	4,4 / 6,4	3,8 / 6,0



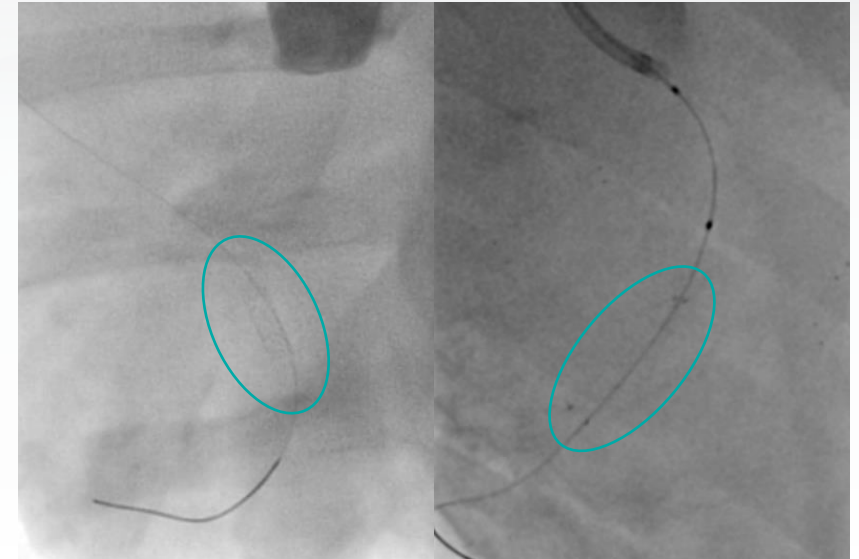
MRI 3.0 T gradient echo image with transversal alignment of stent: L605 (top), Vasculoy (bottom).



- Results superior to 316L
- Results comparable to CoCr – L605

④ Material Properties of Vasculoy® Radiopacity

- Vasculoy® has a similar density/radiopacity like 316L
 - > Recommendation for **radiopaque markers**
 - Two on each stent side
 - No compromises to stent material
 - Good visibility of stent markers (no artifacts)
- Radiopaque materials like PtCr show following disadvantages:
 - High costs
 - Lower strength and strain
 - Less corrosion resistance
 - Artifacts in high resolution angiography (no insight view into stent!)



Angiographical visibility of implanted 316L stent without markers (left) and of a similar stent with markers (right).

Material Properties of Vasculoy®

5 Comparison

- Mechanical Properties:

- Strength 316L < Vasculoy® = L605
- Strain / Plasticity 316L < Vasculoy® = L605

- Corrosion resistance 316L < Vasculoy® >> L605

- Biocompatibility Vasculoy® is the only Ni-free stent material

- MRI compatibility 316L < Vasculoy® = L605

- Radiopacity Radiopaque markers enable good visibility



- The best material for stents and other implants
- The only choice for nickel allergic patients

⑥ Road Map of a Vasculoy® Stent

MeKo's customer support for the development

- **Customer** sends a design identical to an existing L605 stent
- **MeKo** manufactures samples / prototypes (cost < 2000 EUR)
- Initial testing of Vasculoy® stents by **customer**
 - > results will be equivalent to the existing L605 stent
- **Customer** decides for Vasculoy® stent registration:
 - > all necessary biocompatibility data concerning the material will be provided by MeKo for free
 - > documentation support with lots of Ni-allergy literature
- Serial production at **MeKo** for prices like L605 stents



Vasculoy®

List of Literature



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Patient's Safety

Two stents are on the table,
the design and mechanical properties are identical,
one with Nickel, the other without:



Which stent will you take?

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Quality
you can rely on!

