

Novel Magnesium Bioresorbable Scaffold New Insights on Next BRS Technology

**Preclinical evaluation of
drug-eluting bioabsorbable magnesium scaffolds
in a porcine coronary artery model**

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Disclosure

Presenter: Gaku NAKAZAWA

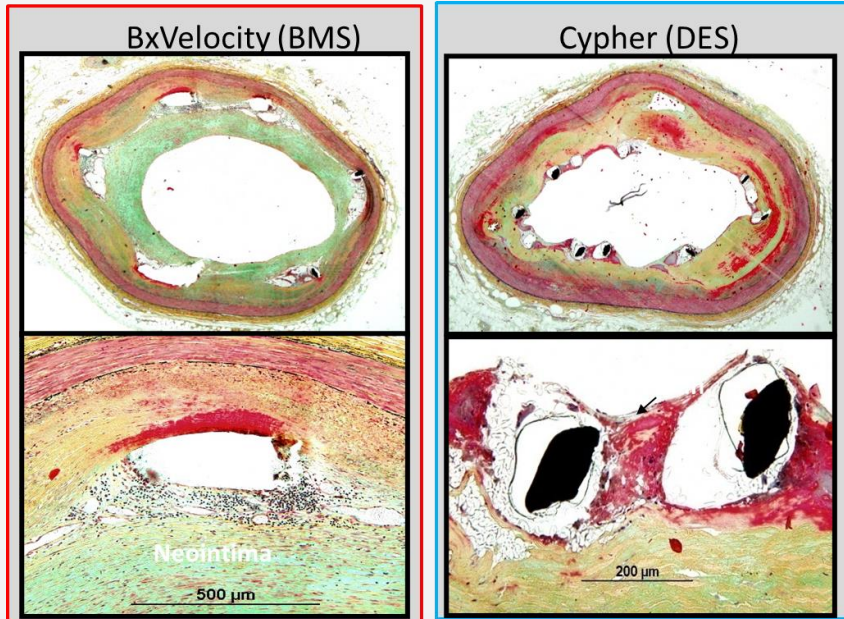
Research fund: Japan Medical Device Technology Co., Ltd. Boston Scientific, Abbott Medical, Terumo Corp.

Honorarium : Boston Scientific, Abbott Medical, Terumo Corp., Daiichi-Sankyo, HeartFlow Japan.

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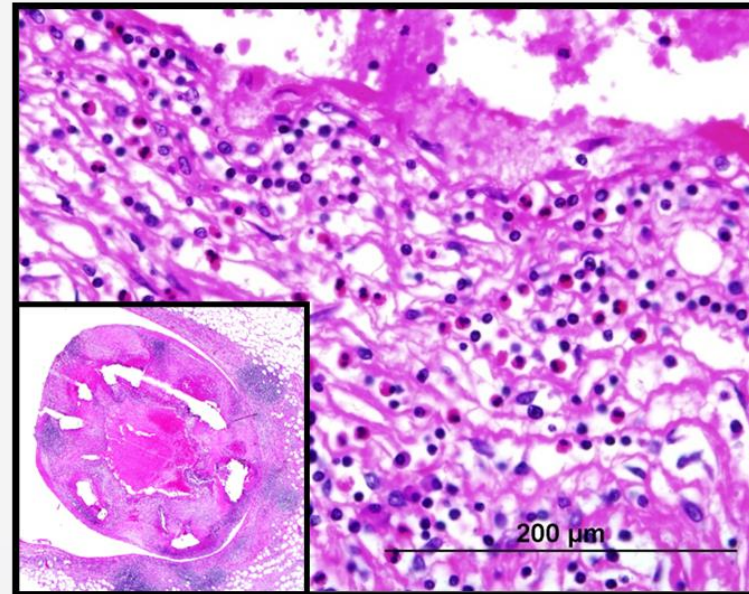
Late Stent Thrombosis – Incomplete Healing is the Major Cause

Delayed Healing



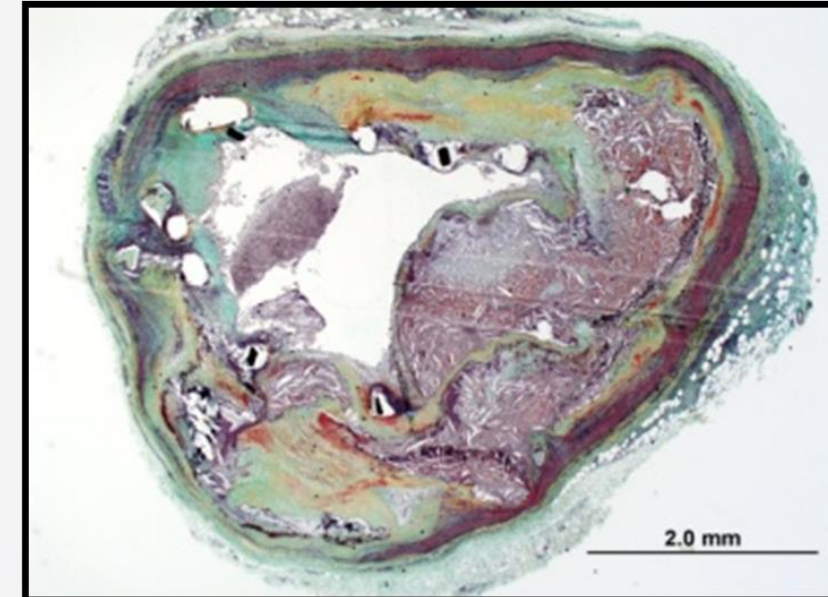
Joner M & Finn AV. J Am Coll Cardiol. 2006;48(1):193-202.

Hypersensitivity



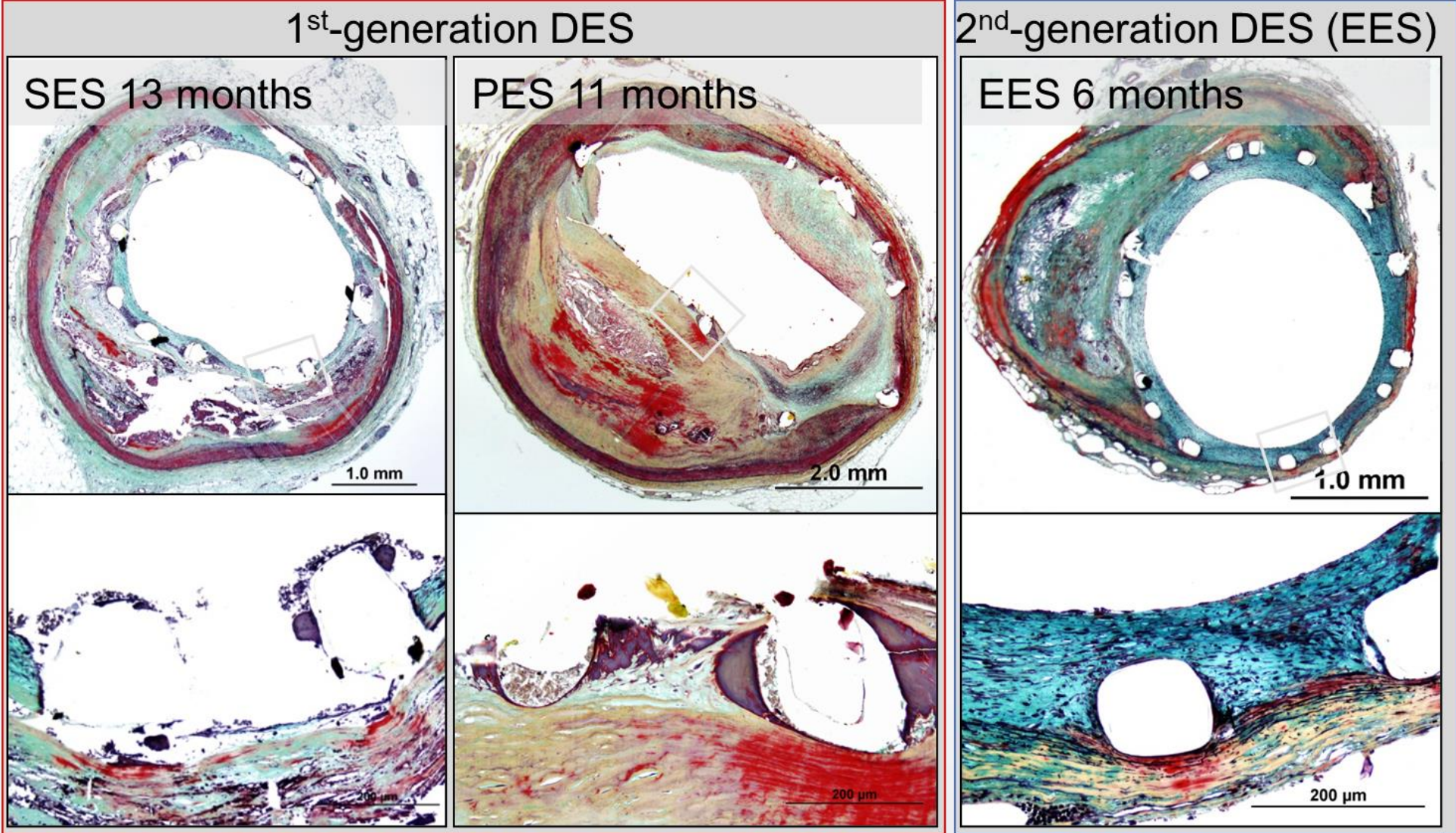
Nakazawa, G et al. J Am Coll Cardiol 2011;57(4):390-8

Neoatherosclerosis

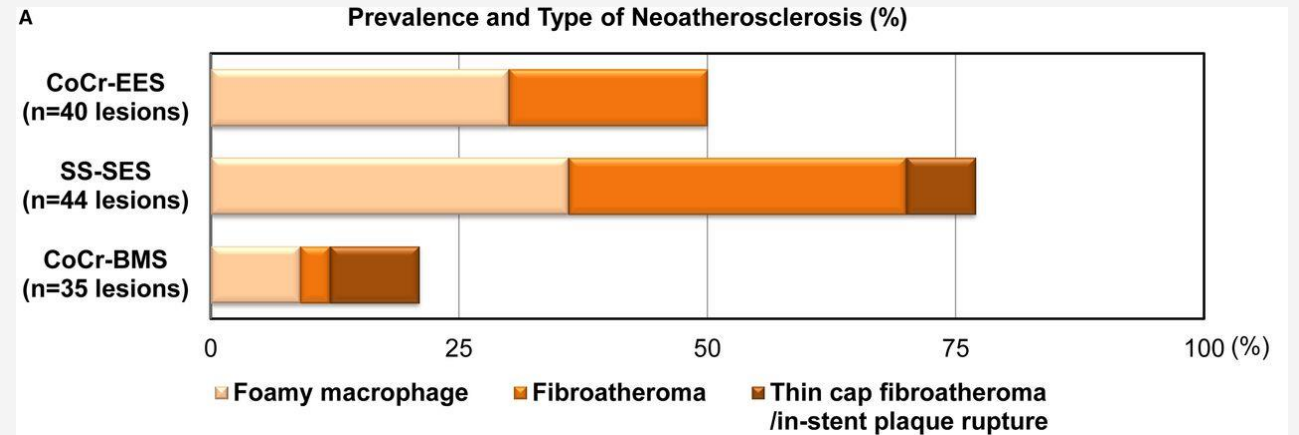
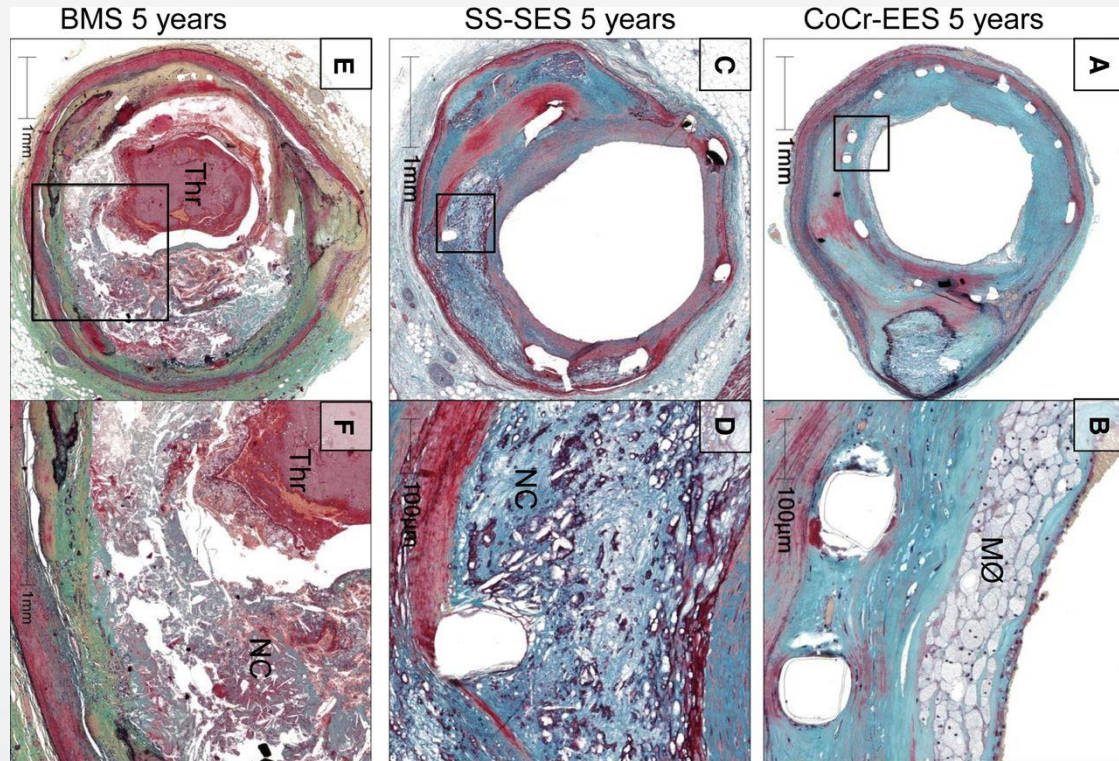


Nakazawa, G & Otsuka, F et al. J Am Coll Cardiol. 2011;57(11):1314-22.

Greater Healing of 2nd Gen DES



Incidence of Neoatherosclerosis (> 5yrs)



Neoatherosclerosis does occur
in 2nd Gen DES

Vascular factor

Endothelial dysfunction
Vulnerability of neointima
Chronic inflammation

Neoatherosclerosis

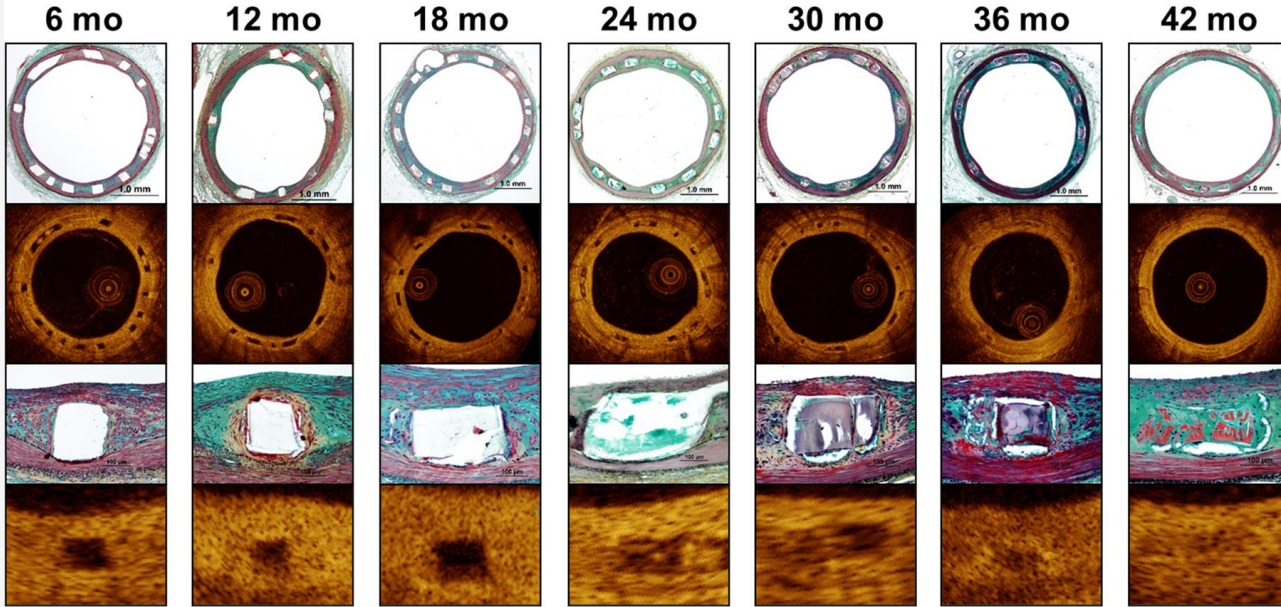
Mechanical factor

Pulsatility
Conformability

Patient factor

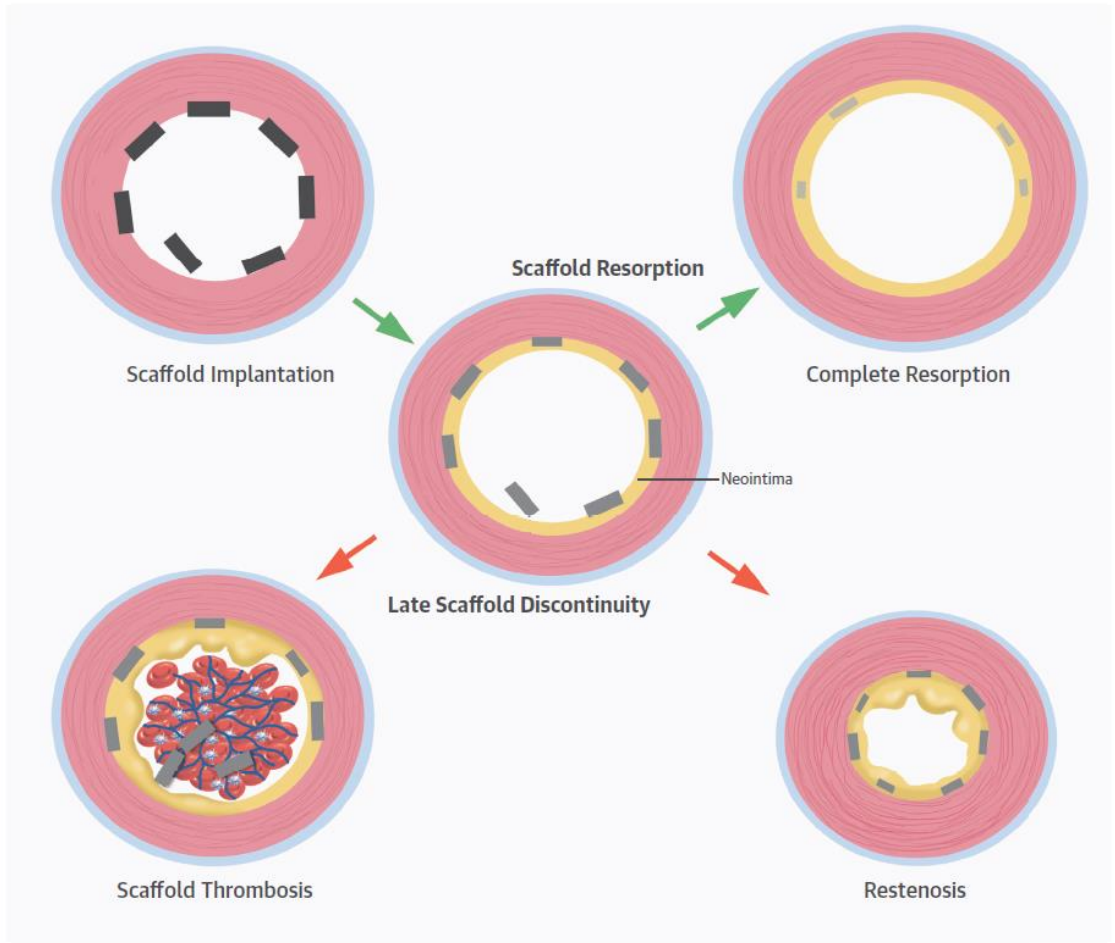
Dyslipidemia
Acute coronary synd

Absorbable devices were expected to solve the mechanical issues



Increased risk of scaffold thrombosis due to late discontinuity

CENTRAL ILLUSTRATION Potential Mechanisms in the Pathogenesis of Very Late Scaffold Thrombosis



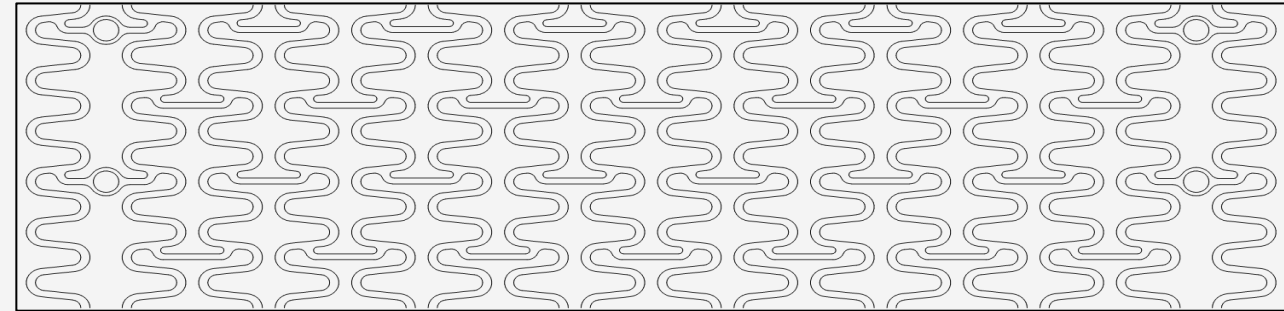
Räber, L. et al. J Am Coll Cardiol. 2015; 66(17):1901-14.

Uneventful scaffold resorption results in positive remodeling with lumen expansion, intact intima, and normal vessel hemodynamics (**upper right**). In the presence of relevant areas of malapposed or uncovered scaffold struts, late scaffold discontinuity may cause dislocation of strut remnants into the lumen. This may lead to disturbed hemodynamic flow and activation of the thrombotic cascade potentially that result in very late scaffold thrombosis (**lower left**). Restenosis in the absence of relevant neointimal hyperplasia represents another potential mechanism in very late scaffold thrombosis (**lower right**).

- The polylactic acid (PLLA)-based bioabsorbable scaffold 'Absorb' has been commercially withdrawn from the market due to high scaffold thrombosis rates resulting from thick struts (150 μm) and long absorption periods (>3 years).
- To overcome these shortcomings of BRS, a novel sirolimus-eluting Mg alloy-based bioabsorbable scaffolds (JFK-01) with thinner struts (110 μm) and shorter degradation rate (2.2 years) was investigated.

Characteristics of JFK-01

Material	Magnesium (free of rare earth metals)
Strut thickness	110 μm
Profiles width	1.2-1.3 mm
Percent of area in contact with vessel wall	17.4 %
Flexibility	5.46 mN^{-1}
Initial strength	60-70 N/mm
Drug dose (3.0X20mm)	1.0 $\mu\text{g}/\text{mm}^2$



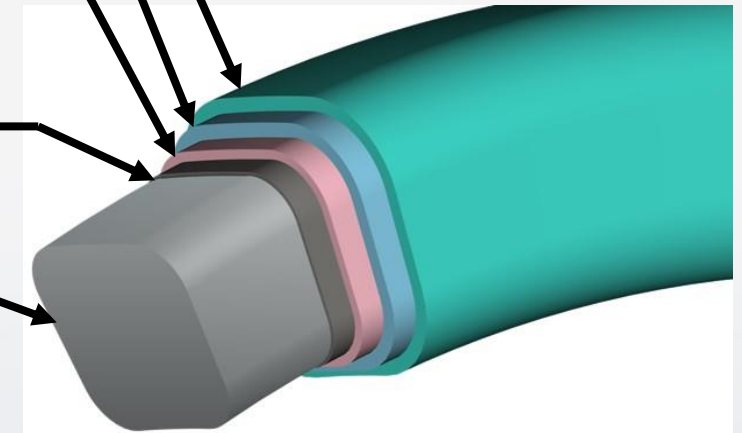
2nd layer (PDLLA + Sirolimus)

1st layer (PLCL/PCL)

Parylene C

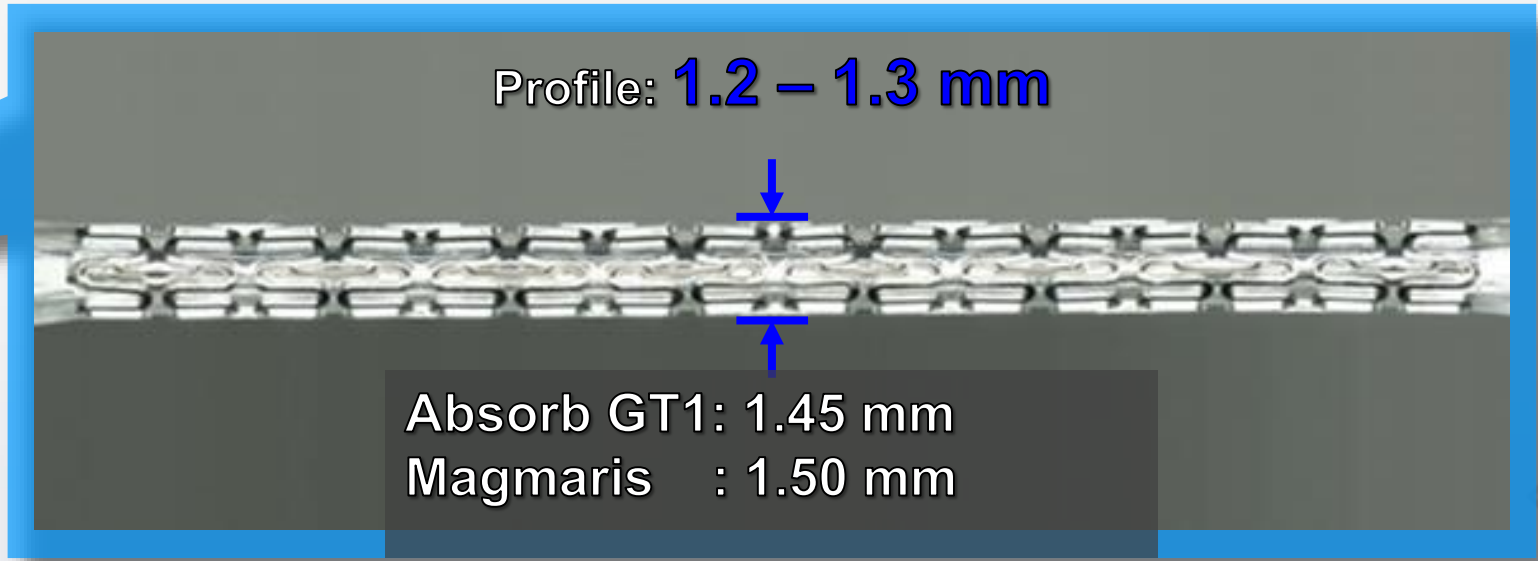
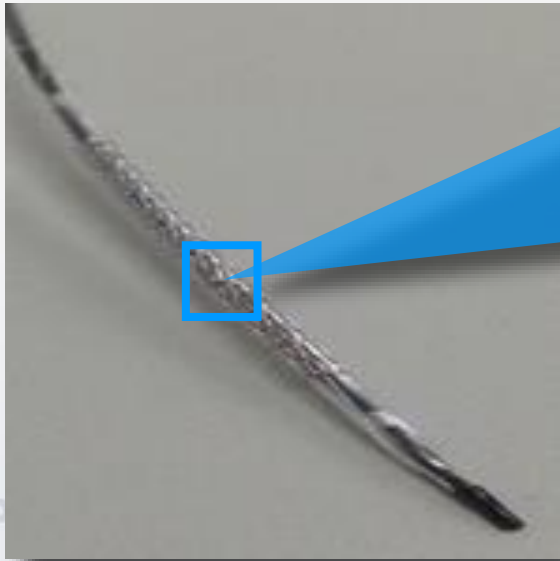
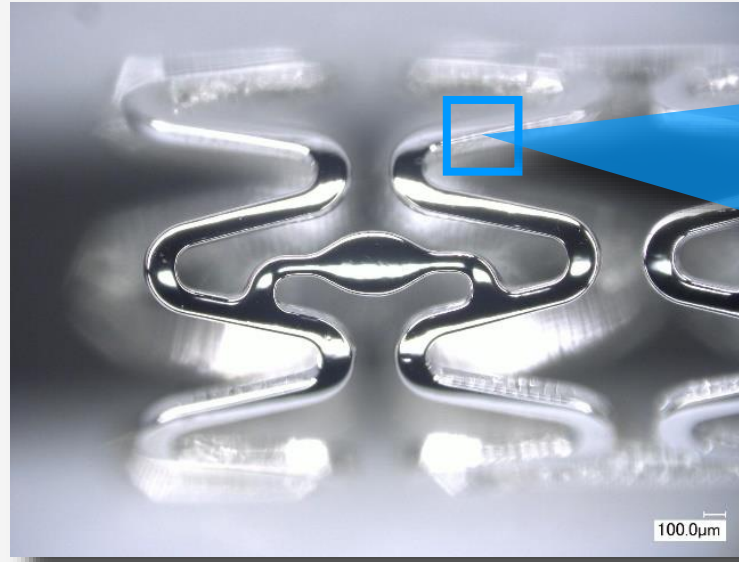
Fluoride-based layer

RE-free Mg alloy



3.0x20mm

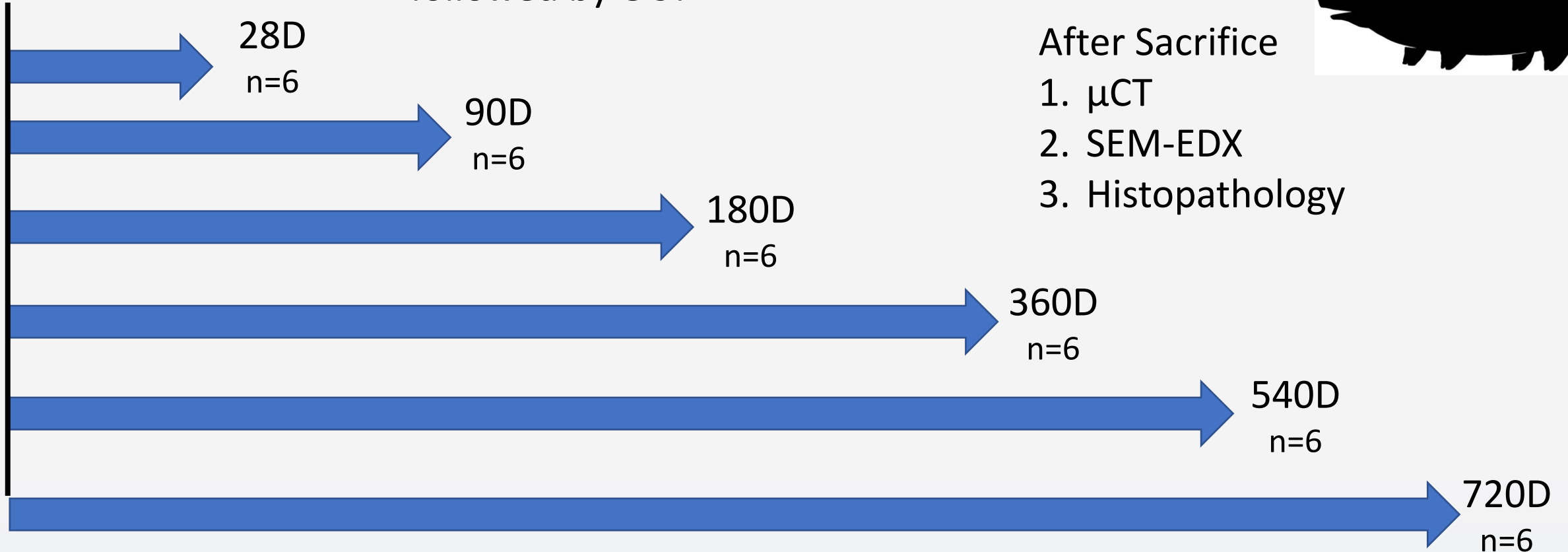
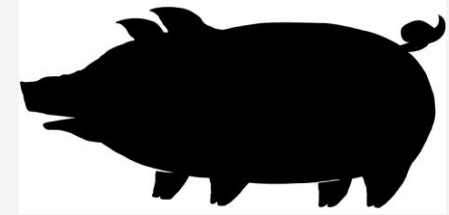
Bioresorbable Mg alloy-based scaffold (JFK-01)



Method of JFK-01 GLP Survival

Initial procedure

JFK-01 3.0/20 mm implantation followed by OCT



After Sacrifice

1. μ CT
2. SEM-EDX
3. Histopathology

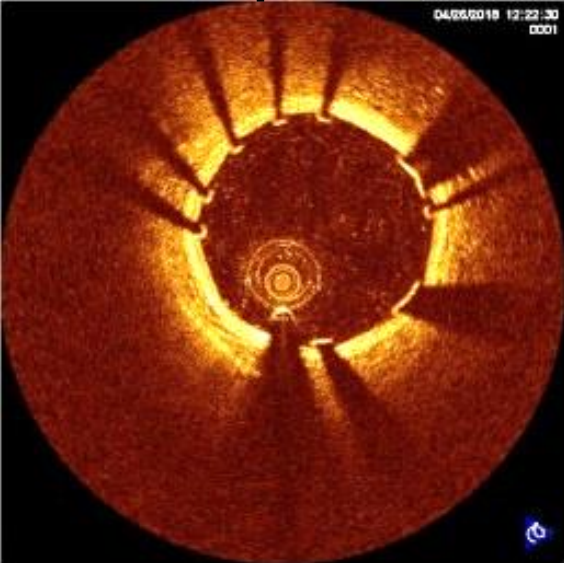
follow-up

1. Angio
2. OCT



Representative pictures of serial OCT images of JFK-01

Post implantation



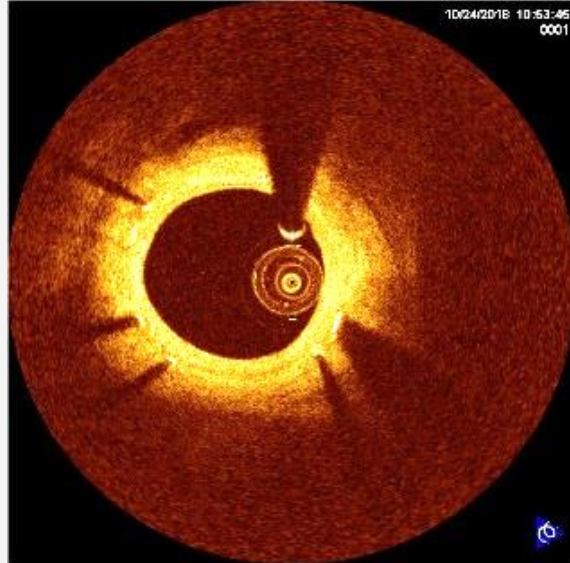
1M



3M



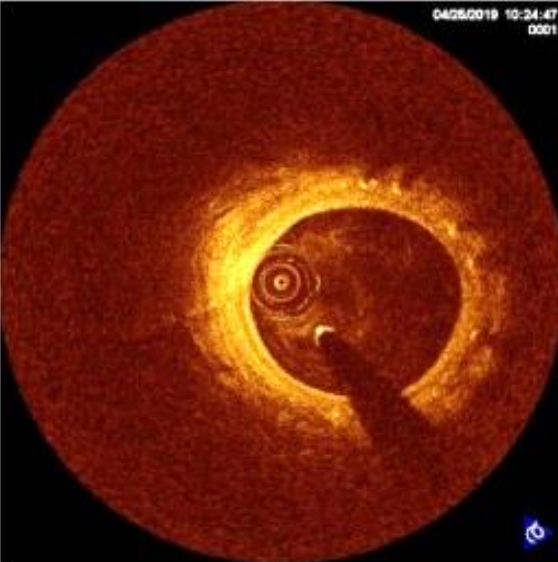
6M



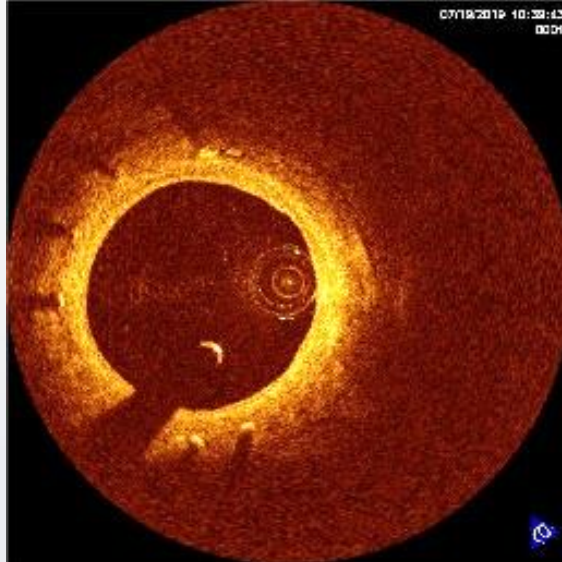
9M



12M



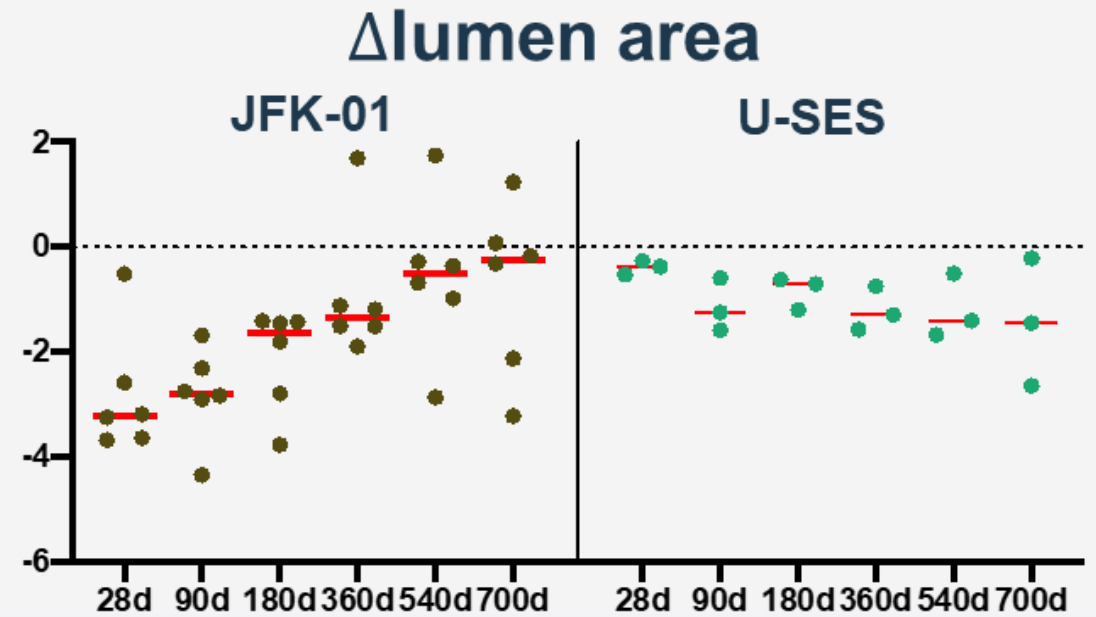
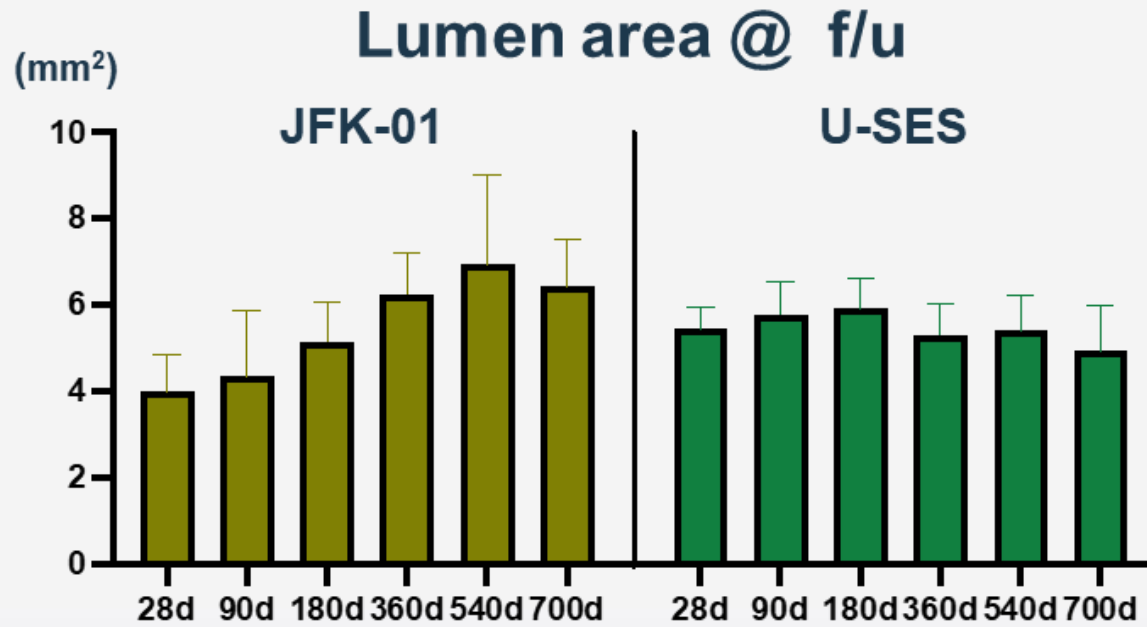
18M



26M

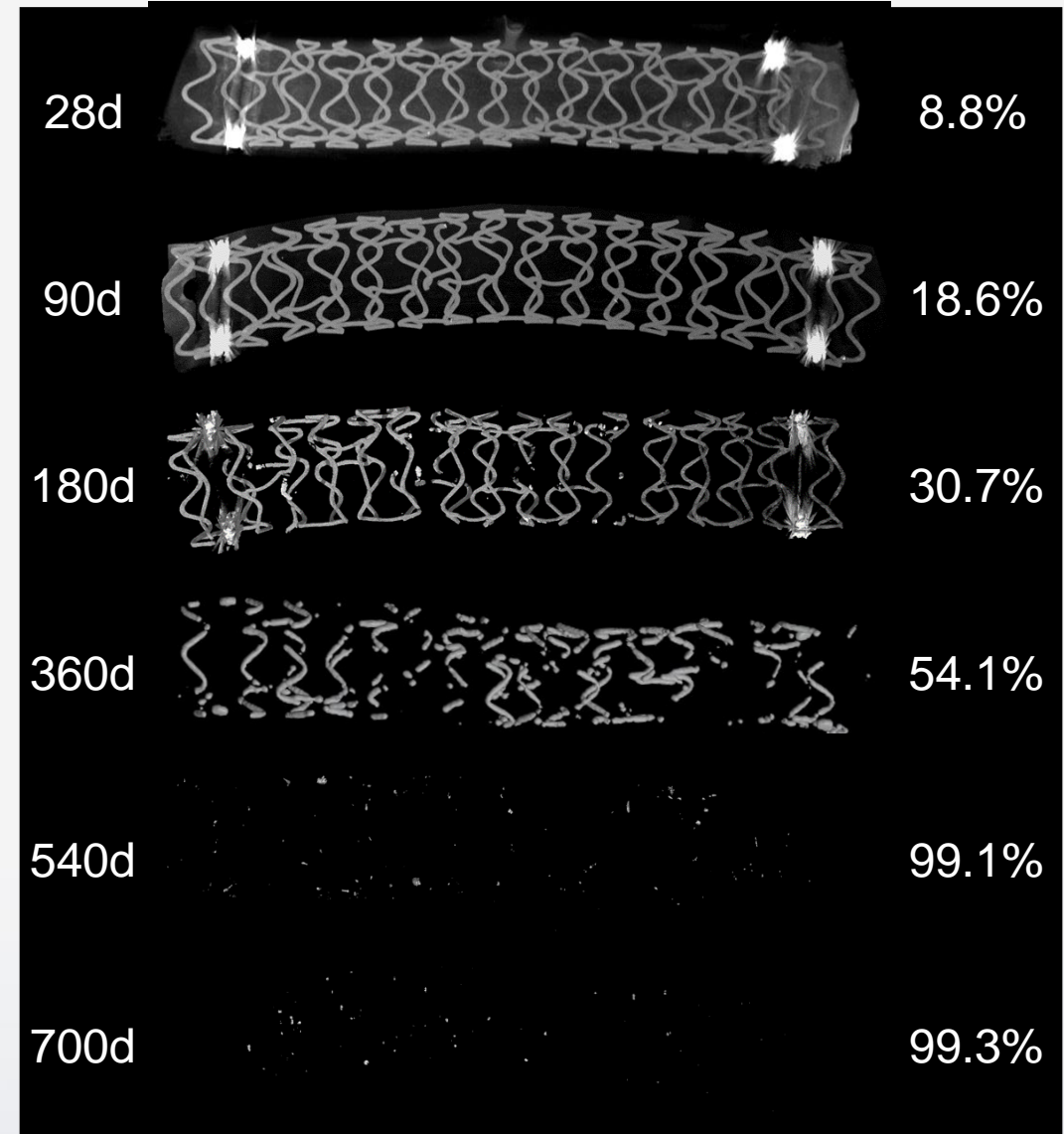
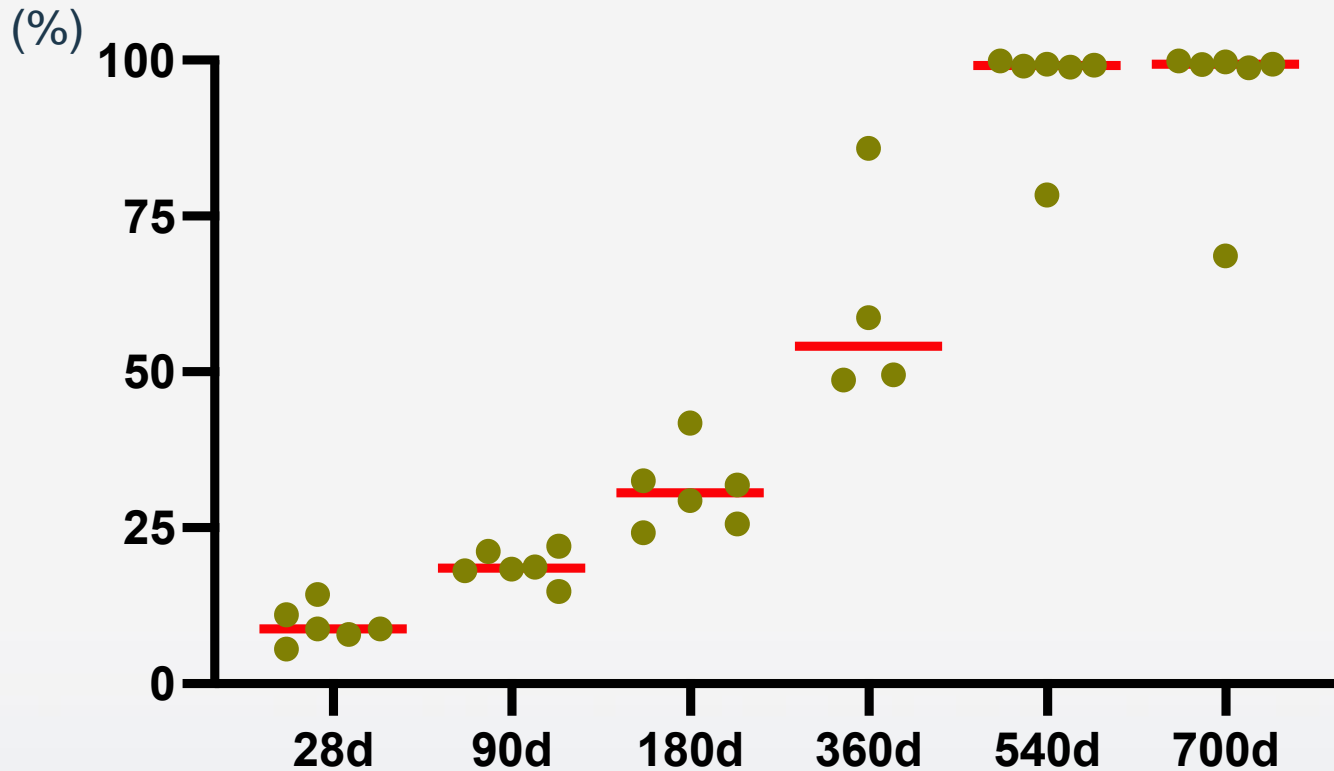


OCT analysis



Micro CT analysis of the implanted Mg scaffold

Percentage of degraded scaffold volume



Representative histologic sections

28d

90d

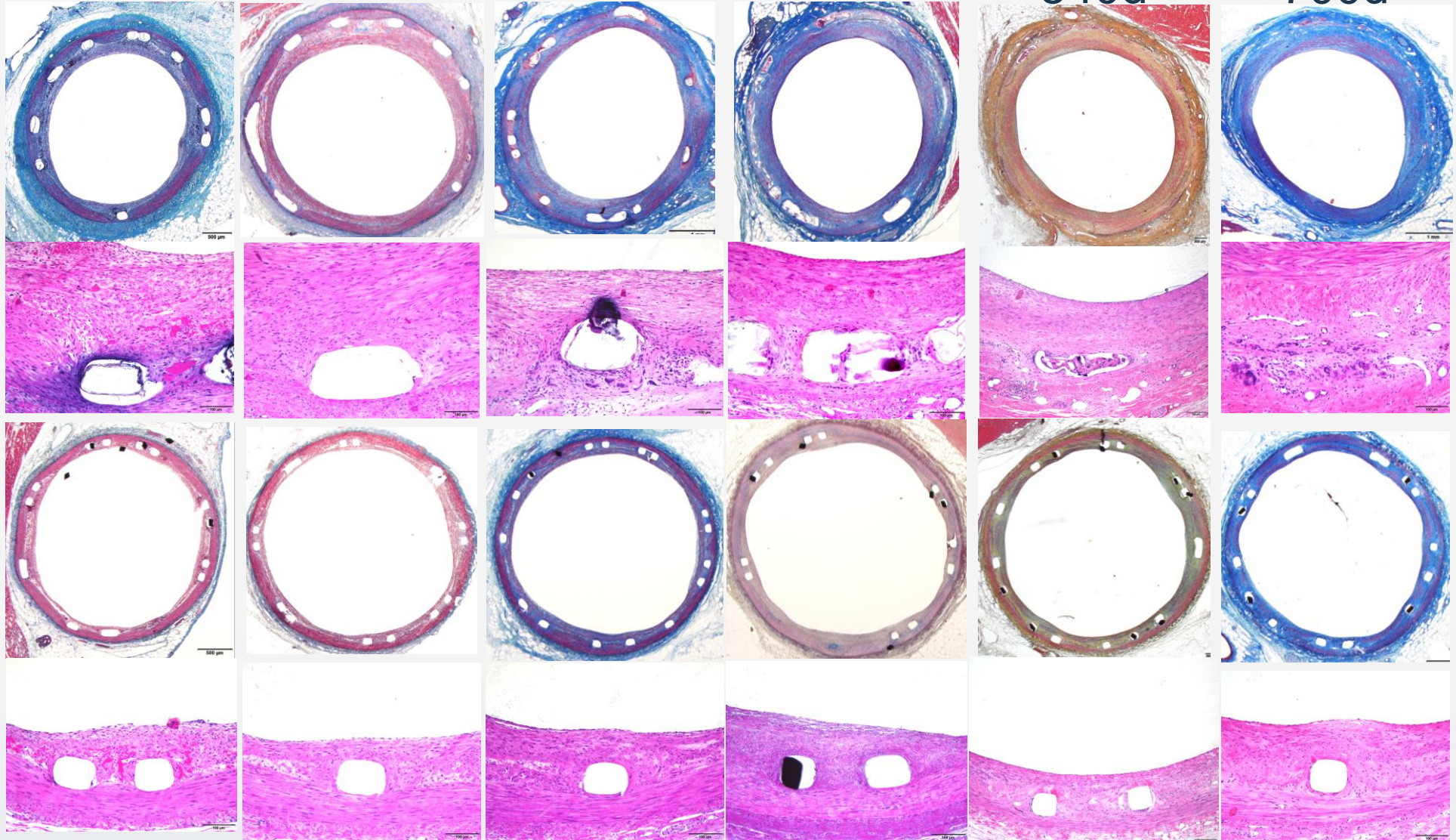
180d

360d

540d

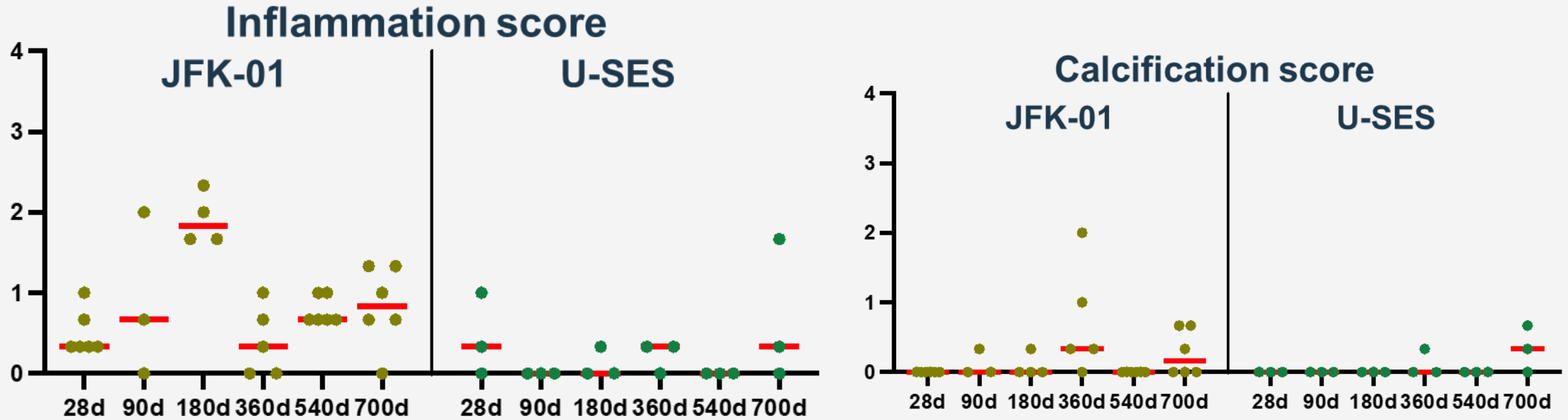
700d

JFK-01



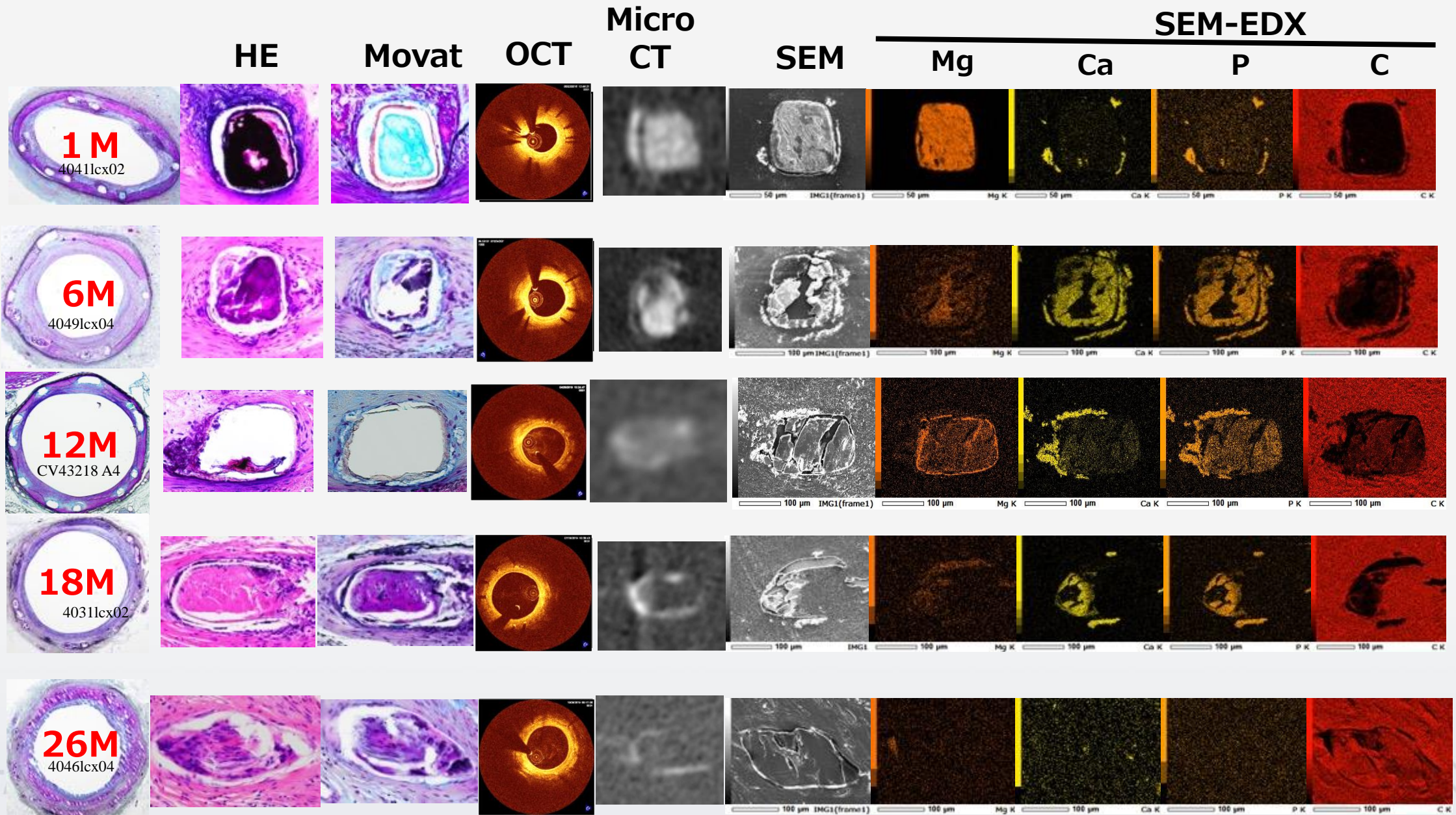
U-SES

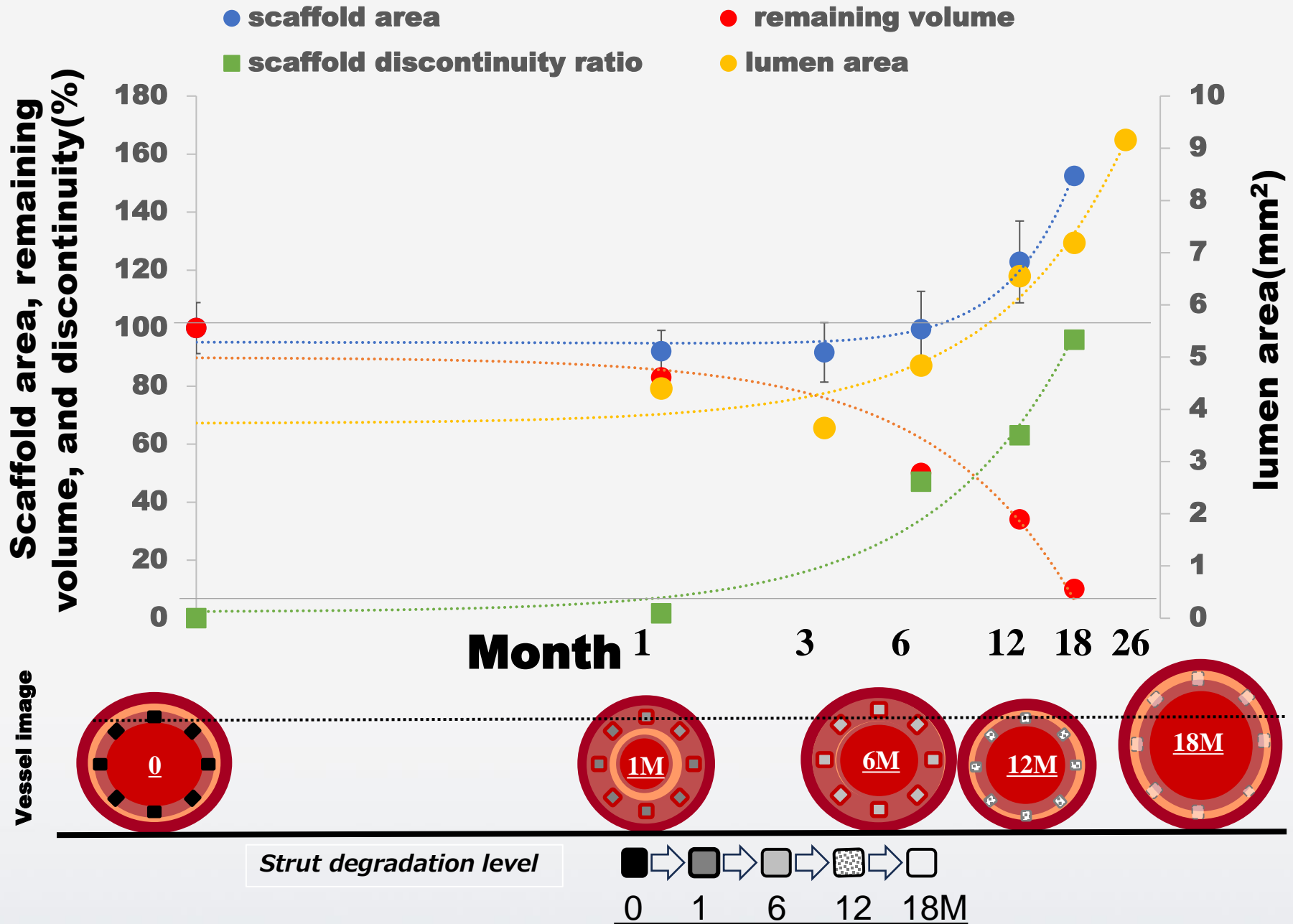
Pathological evaluation



- Inflammation peaks at 180d in JFK-1 and decreased thereafter
- Calcification was observed but not extensive

Co-registration of histology, OCT, uCT, and SEM-EDX





- **OCT analysis demonstrated that there was no acute recoil, and the vascular patency was maintained throughout the study in all the scaffolds implanted.**
- **Vessel enlargement was observed at 15 M after scaffold implantation , and the trend was further augmented at 18, 24, and 26 M.**
- **Inflammation peaked at 18M and decreased thereafter.**

- **μ CT, SEM-EDX, and histopathological analysis demonstrated that degradation of the Mg alloy backbone was confirmed at 6M with partial substitution of the Mg alloy strut by insoluble substances containing Ca and P.**
- **Further degradation with strut discontinuity was observed at 12M, and final replacement by carbon suggests complete resorption of the Mg alloy backbone at 26M.**

Progress of FIH testing of JFK-01

- **Scientific Title:** An Exploratory Multicenter, Open-Label Clinical Study to Evaluate the Safety and Efficacy of JFK-01 (Coronary Artery Absorbable Magnesium Alloy Scaffold) in Patients with Ischemic Heart Disease
- **Contact for Scientific Queries /Name :** Gaku Nakazawa
- **Affiliation :** Kindai University Hospital
- **Anticipated date of first enrollment :** Jan. 12, 2023
- **Target sample size : 30**
- **Key inclusion & exclusion criteria /Inclusion Criteria:**
 1. **De Novo Coronary Lesions**
 2. One lesion or two lesions in one or two branches that are eligible for PCI
 3. Lesions with visual diameter stenosis (AHA stenosis classification) greater than 75% and less than 100%.
 4. Lesions with TIMI classification grade 1 or higher blood flow
 5. **Lesions with a vessel diameter of 3 mm and lesion length of 18 mm or less**

Progress of FIH testing of JFK-01

- **FIH participating 10 facilities:**
Iwate Medical University Hospital,
Teikyo University Hospital
Mitsui Memorial Hospital
Tokai University Hospital
Fujita Medical University Hospital
Kindai University Hospital
Kurashiki Central Hospital
Kokura Memorial Hospital
Kurume University Hospital
Kumamoto University Hospital



➤ **17 cases included (202404)**

- **In the current preclinical study, the novel bioresorbable drug eluting Mg alloy scaffold system, JFK-01 demonstrated safety features with controlled degradation of the Mg alloy backbone (2.2 years), resulting in long term vessel enlargement with its complete resorption.**
- **First in Human trial is ongoing and enrollment will be completed Q4 2024.**