THE FIRST REPORT ON CHARACTERISATION OF PARTIALLY COVERED SELF-EXPANDABLE METALLIC STENTS IN ESOPHAGEAL CANCER TREATMENT: *IN VIVO* DEGRADATION

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Introduction
Squamous cell carcinoma of the esophagus is the fourth cause of death in males and seventeenth in females. There is no change or slight decrease in incidence over the last three decades [1]. More than 50% of patients present with unresectable tumour, progressive weight loss and dysphagia require palliative treatment. Among the many available methods of palliation, stenting, laser therapy, chemoradiation, and photodynamic therapy are considered. However, most often stenting is the method of choice. This is because of technical simplicity, wide availability and immediate alleviation of dysphagia.
Patients requiring stenting are usually diagnosed with III and IV grade dysphagia and significant weight loss. The stents that are currently used, despite relative good tolerance, are not free from side-effects and complications. One of the most common problems associated with stenting is granulation tissue overgrowth and stent obstruction. Coverage with a polyurethane or silicone membrane protects from tumour ingrowth, but overgrowth beyond ends of the stent and granulation tissue formation remains an issue.
The aim of the study was to investigate the impact of long-term usage in the body on physicochemical properties of partially-covered esophageal stents.

Materials and Methods
Structural analysis of 16 partially covered self-expandable metallic stents (SEMS) has been subjected after removal due to their dysfunction. SEMS were implanted because of dysphagia as a result of inoperable esophageal cancer or before chemo-radiotherapy such as bridge to radical surgery treatment. Prostheses have been removed because of their obstruction and recurrence of dysphagia which make oral nutrition impossible for patients.
For the investigations, partially covered SEMS 7–12 cm long and with diameter of 18 mm (Ultraflex Boston Scientific, Natick, MA, USA) were used. For the physicochemical investigation, the obtained stents were cut into 1x1 cm coupons. The morphology of the NiTi stent and polyurethane covering surfaces were evaluated by a Hitachi S-4700 scanning electron microscope (SEM). The properties of polymeric samples were analysed using a TGA/DTA Mettler-Toledo apparatus. The polymeric samples of about 1 mg were placed in an open alumina crucibles. The measurements were carried out in a temperature range of 30–600°C with a heating rate of 5°C min^{-1} at an Ar flow of 50 cm^3 min^{-1} [2]. The changes within the surface of polyurethane were followed by contact angle measurements (CA), using a Surftens universal instrument (OEG GmbH) equipped with Surftens 4.3 Windows image processing software. For each sample, 5 independent 1 μL water drops were applied [3]. ATR-FTIR analyses of the polymeric films were performed on a Spectrum 100 Nicolet 6700 (Thermo Scientific). The spectra were recorded in at least 3 independent spots at the samples in the range 4000–650 cm^{-1}.

Results and Discussion
Structural analysis has been subjected of 16 removed prostheses from patients (3 women and 13 men aged 40-80) which were treated in the course of squamous cell carcinoma (14 patients) and adenocarcinoma of the esophagus (2 patients). Among the treated patients 5 received chemo or chemo-radiotherapy, 5 preoperative chemo-radiotherapy, 6 did not receive treatment.
The SEM observations revealed surface changes on the metal alloy, mostly cracks, on the used esophageal stents when compared to the reference sample. The changes in surface morphology of polyurethanes covers were also visible – the damage of the surface was mostly due to cracks and peeling off 5–10 μm polymeric fragments. The degradation of the polyurethane films was confirmed with ATR-FTIR, indicating the significant loss of intensity at 2930 cm^{-1}, 2860 cm^{-1}, 1740 cm^{-1}, and 1245 cm^{-1} which correspond to the functional groups $–CH_2$, C=O, C-N, respectively. It is worth mentioning that the degradation of polymers was greater at the distal end of the stent. The highly probable reason for that is the more acidic environment nearby the stomach when compared to the proximal end. The bulk changes in the polymer structure before and after stent implantation were compared in terms of melting temperature (T_{melt}). The T_{melt} for the distal end of the investigated stents were shifted of ≈ 20°C towards higher temperatures which indicates significant bulk changes in the polyurethane covers exposed to the human body environment.

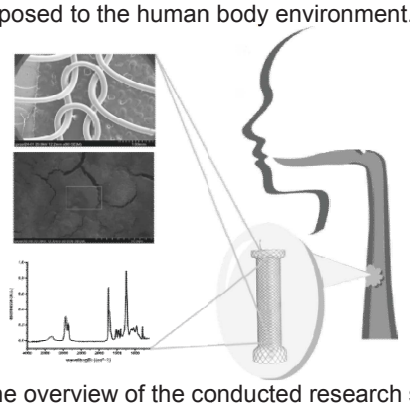

FIG. 1. The overview of the conducted research strategy.

Conclusions
The 16 esophageal stents (Nitinol-polyurethane) were examined after prolonged usage in the body. Physicochemical characterization (SEM, ATR-FTIR, TG/DTA, CA) revealed significant changes in the materials bulk (T_{melt}) and surface morphology as well as surface functional groups (CA, IR). It was concluded, that the degradation strongly depends on the physiological environment (i.e. medical treatment, in-site pH). The main directions for improvement of the stents were pointed out.

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