BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

UNITO - DAEDALUS 1 - Artificial Intelligence, robotic mucosectomy and in situ bioprinting for regeneration of ColoRectal mucosa and submucosa

Funded By	UNIVERSITA' DEGLI STUDI DI TORINO [P.iva/CF:02099550010]

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Context of the research activity	Artificial Intelligence, robotic endoluminal surgery and in situ bioprinting for regeneration of ColoRectal mucosa and submucosa in dysplastic and inflammatory diseases

	The University of Turin is a partner of an international consortium for a Horizon Europe Research Project called DAEDALUS on the development of a ADvAnced 4D biomAteriaLs for mucosa and sub-mUcosa treatment in patients affected by intestinal diseases. DAEDALUS has the ambitious goal to change the landscape in the surgical treatment of Familiar Adenomatous Polyposis and Ulcerative Colitis, by providing a minimally invasive breakthrough solution based on an in situ bioprinting strategy to 4D bioprint personalized shape morphing GMP-compliant bioconstructs through an endoscopic/endoluminal procedure. Based on the knowledge and previous results of DAEDALUS partners (e.g., design of printing systems, in situ bioprinting, path planning, 4D bioprinting, endoscopic colorectal surgery, cell biology, biomaterial synthesis and functionalization, regulatory pathways) the project will start from a TRL 3-4 and in four years it will develop: i) an in situ bioprinting apparatus, referred to as a colonoscopic bioprinter, comprising both hardware and software for bioprinting control; ii) AI-empowered in silico tools able to plan the 4D bioprinting process according to the patient defects and the required advanced functionalities (e.g., drug release); iii) advanced biomaterials, comprising collected and expanded patient cells and biomaterials for mimicking the mucosa and submucosa layers and for delivering active pharmaceutical ingredients (API). Both the in situ bioprinting apparatus, the bioinks, and the functionalization biomaterial ink will be tested and validated in a relevant environment by

Objectives	colorectal surgeons inside the consortium (TRL 5-6), and their commercial scale-up will be proved by the industrial partners. The treatment of the affected colorectal area envisioned in DAEDALUS involves firstly the surgical removal of only the diseased mucosa and submucosa layers, through a minimally invasive procedure that preserves the underlying muscular layers, followed by the in situ 4D bioprinting of the submucosa and mucosa layers. These two layers will be obtained by precisely depositing light-sensitive bioinks through extrusion-based bioprinting (EBB). Subsequentially, they will be functionalized via valve-jet printing (VJP) of micro- and nano-carriers to deliver API. A 4D shape morphing process, supported by a shape memory melt-electro written (MEW) tubular grid and a differential swelling of the mucosa layer, will allow to biomimic the crypt-like morphology of mucosa. To achieve this ambitious innovation, DAEDALUS will target four specific objectives (SOs): SO1: To synthesise two novel cell-laden 4D composite biomaterials with advanced functionalities for the substitution of colorectal mucosa and submucosa SO2: To boost the development of new advanced biomaterial formulations via in silico tools. SO3: To introduce a novel minimally invasive surgical treatment for patients affected by FAP or UC based on advanced 4D composite biomaterials. SO4: To create the conditions for a successful scale-up, user acceptance and exploitation of the DAEDALUS solution after the end of the project Here, we focus on SO3. DAEDALUS biomaterials are meant to be used for the reconstruction of both colorectal mucosa and submucosa after their surgical removal in patients affected by FAP or UC. In the minimally invasive procedure, we envision the removal of the injured mucosa and submucosa followed by in situ injection of the cell-laden 4D composite biomaterials over the damaged area employing a customized endoscope. DAEDALUS will deliver an ad hoc engineered multifunctional tool head mounted on a commercial endoscope that will include tools for: i) in situ delivery (multi-orifice extrusion system enabling control over volume and area of delivery; a multipurpose hole for dispensing the tubular grid via a deposition balloon, microfluidic-based mixing system to generate gradients), ii) crosslinking (light), and iii) actuation (magnets/light). The multifunctional tool head will be designed and fabricated to be mountable on commercial endoscopes at different scales (human/swine and mouse) and will be tested both ex vivo and in vivo. UNITO will be responsible for the identification of the design constraint of the 3D bioprinting procedure from a clinical point of view, of the data collection of images during colonoscopies of patients affected by FAP and UC, and of performing the complete procedure on phantoms, ex vivo test on swine models and human corpses. UNITO will be responsible for testing on phantoms the bioprinter using GMP-compliant bio-inks

Skills and competencies for the development of the activity	Applicants must hold a Master's degree in Bioengineering with expertise in robotics and computer vision for endoluminal applications. Essential skills include proficiency in one or more areas: control of actuator and robotic arm (i.e. KUKA, Franka, Universal Robot), CAD design and prototyping, expertise in sensor usage, data analysis and knowledge of program languages (i.e. C++). Relevant scientific publications and ethical committee expertise are advantageous.