FINAL REPORT OF THE ENIUS COST ACTION. 2017-2022.

MOU OBJECTIVES ASSESSMENT.

The first step to conclude our COST Actions is to assess the achievement of our objectives. These are the objectives of ENIUS, as described in the MoU that was approved by the CSO.

Research Coordination Objectives

Objective 1. To determine the causes of failure and side effects of urinary stents from the clinical point of view and industrial design. This objective has been achieved and is included in four chapters of the book coordinated by WG1. "*Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaf editors. OA Springer Nature, 2022*".
Chapter. 1. Present and Future of urinary stents. F. Soria.
Chapter. 2. Indications, complications and side effects of ureteral stents. D. Pérez-Fentes, J. Aranda, J de la Cruz, F. Soria.
Chapter. 3. Indications, complications and side effects of metallic ureteral stents. D. Rako.
Chapter. 4. Indications, complications and side effects of urehral stents. de Graaf P, Yachia D, Soria F, Rako D.

Objective 2. Develop multidisciplinary guidelines for the evaluation and validation new stent designs at computational, experimental and preclinical level.

This objective has been achieved, we have developed multidisciplinary guidelines to new urinary stents assessment and validation. Our guidelines and White papers has been detailed in 3 scientific papers and three chapters of the book coordinated by WG1 "Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022".
-Scientific paper WG2-3-6. Buchholz N, Budia A, de la Cruz J, Kram W, Humphreys O, Reches M, Soria F, Valero R. Urinary stent development and evaluation models: in-vitro, ex-vivo and in-vivo. A European Network of

Multidisciplinary Research to Improve Urinary Stents (ENIUS) Initiative. Polymers, 2022. OA.
-Scientific paper WG6. Abou-Hassan A, Barros A, Buchholz N, Carugo D, Clavica F, de Graaf P, de La Cruz J, Kram W, Mergulhao F, Reis RL, Skovorodkin I, Soria F, Vainio S, Zheng S. Potential strategies to prevent encrustations on urinary stents and catheters - thinking outside the box: a European network of multidisciplinary research to improve urinary stents (ENIUS) initiative. Expert Rev Med Devices. 2021;18(7):697-705. OA.
-Scientific paper WG2. Zeng S, Carugo D, Mosayebi A, Turney B, Burkhard F, Lange D, Obrist D, Waters S, Clavica F. Fluid mechanical modelling of the upper urinary tract. WIREs Mech Dis 2021;e01523. OA.
-Chapter. 14. Flow dynamics in stented ureter. Zheng S, Carugo D, Clavica F, Mosayebi A, Waters S. In Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022.
-Chapter 15. Methodology for the development and validation of new stent designs: in vitro and in vivo models. Kram W, de la Cruz JE, Owen H, Buchholz N, Soria F. In Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022.
-Chapter 16. Methodology on clinical evaluation of urinary stents. S. Sotir, M. Sofronievska. In Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022.

Objective 3. Assess opportunities for improved stents related to the assessment of new biomaterials, new coatings, drugs eluting stents. This aim has been achieved, due to the great work of WG4 and 5.
The findings of the different WGs involved have been described in 16 chapters & 14 papers. As well as a link from our website to a database: Urinary Stents.Info Meeting point. www.enius.org.
-Chap. 9. Ureteral stent designs to reduce morbidity: anti-reflux stents, intraureteral stents, bladder-end tail stents. de la Cruz JE.
-Chap. 17. A Dynamic Surface: Can We ‘Fool’ Bacteria to Delay Biofouling in Urinary Stents ? S. Tofail.
-Chap. 18. Biomaterials for ureteral stents: advances and future perspectives. Pacheco M.
-Chap 19. Coatings for urinary stents:current state and future directions. Domingues B.
-Chap 20. Bacterial adhesion and biofilm formation: hydrodynamics effects. Gomes LC.
-Chap 22. Biomaterial-associated infection: pathogenesis and prevention. Riool M.
-Chap 23. Antibiotic-free solutions for the development of biofilm prevention coatings. Costa B.
-Chap 24. Plasma Based Approaches for Grafting of Antimicrobial Agents to Polymer Surfaces. Vladkova TG.

Chap 25. Antimicrobial biosurfactants towards the inhibition of biofilm formation. Anjos I.
-Chap 27. Light activated polymer nanocomposites doped with new type of hydrophobic carbon quantum dots for antibacterial applications. Kováčová M.
-Chap 29. Urinary tract infections and encrustation in urinary stents. Herout R.
-Chap 31. Biodegradable urinary stents. Soria F.
-Chap 32. New double-J stent design for preventing/reducing irritative bladder symptoms & flank pain. Yachia D.
-Chap 33. Drug eluting stents in urinary stents. Kallidonis P.
-Chap 35. Techniques to create Drug eluting stents. Carmagnola I.
-Chap 37. Ten steps to strategic planning for the urinary stents of the future. Soria F.
-Laurenti M.Porous ZnO2-hydroxyethyl Metacrylate eluting coatings for ureteral stent applications. Coatings 2018, 8(11):376.
-Venkatesh C. Biodegradation and antimicrobial properties of Zinc oxide-polymer composite materials for urinary stent applications. Coatings 2020;10 (10);1002.
- ENIUS. European Network of multidisciplinary research to Improve the Urinary Stents. COSTS Actions. CA16217. European Cooperation in Science & Technology. Urolithiasis. 2020 Dec;48(6):553-559.
-Staneva A. Preparation and antimicrobial activity of collagen/(RgO/ZnO/TiO2 /SiO2) composites. Journal of Chemical Technology and Metallurgy, 55, 5, 2020, 1078-1086.
-Laurenti M. Biodegradable and Drug-Eluting Inorganic Composites Based on Mesoporous Zinc Oxide for Urinary Stent Applications. Materials (Basel). 2020 Aug 29;13(17):3821.
-Alves P. Analysing the initial bacterial adhesion to evaluate the performance of antifouling surfaces. Antibiotics, 2020.
-Gomes M. PDMS in urinary tract devices: Applications, problems and potential solutions. Polydimethylsiloxane: Structure and Applications, 1 st ed; Carlsen, PN, 2020.
-Alves P. The potential advantages of using a poly (HPMA) brush in urinary catheters: Effects on biofilm cells and architecture. Colloids and Surfaces B: Biointerfaces, 2020.
-Gospodinova D. Fabrication and Characterization of Antimicrobial Magnetron Computered TiO2/Ag/Cu Composite Coatings. Coatings, 2021.
-Zmejkoski DZ. Bactericidal and antioxidant bacterial cellulose hydrogels doped with chitosan as potential urinary tract infection biomedical agent. RSC Adv., 2021,11, 8559-8568.
-Zeng S, et al. Fluid mechanical modelling of the upper urinary tract. WIREs Mech Dis 2021;e01523.
-Abou-Hassan A,et al. Potential strategies to prevent encrustations on urinary stents and catheter -thinking outside the box: a European network of multidisciplinary research to improve urinary stents (ENIUS) initiative. Expert Rev Med Devices. 2021;18(7):697-705.

-Domingues B. Future Directions for Ureteral Stent Technology: From Bench to the Market. Advanced Therapeutics, 2022.
-Shaokai Z. Quantitative Evaluation of Encrustations in Double-J Ureteral Stents With Micro-Computed Tomography and Semantic Segmentation. Frontiers in Urology, 2022.

Objective 4. To develop a realistic computational environment to assess the Computational simulation and modelling and computational fluid dynamics to evaluate new urinary stents designs. This is an overly ambitious goal that we modified and changed according to the advice of WG2 leaders. It was changed by a database, and scientific papers.

-Scientific paper WG2. Zeng S, Amado P, Kiss B, Stangl F, Haeberlin A, Sidler D, Obrist D, Burkhard F, Clavica F. Quantitative Evaluation of Encrustations in Double-J Ureteral Stents With Micro-Computed Tomography and Semantic Segmentation. Frontiers in Urology, 2022.
-Scientific paper WG2. Zeng S, Carugo D, Mosayyebi A, Turney B, Burkhard F, Lange D, Obrist D, Waters S, Clavica F. Fluid mechanical modelling of the upper urinary tract. WIREs Mech Dis 2021;e01523.
-Chapter 14. Flow dynamics in stented ureter. Shaokai Zheng, Dario Carugo, Francesco Clavica, Ali Mosayyebi, Sarah Waters. In "Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022".

Objective 5. **Stimulate innovative scientific ideas and propose new lines of research and technological innovation in the field of urinary stents**. This objective has been achieved, a multitude of activities (TS and Workshops) have been developed to reach agreement on ideas to improve urinary stents from a multidisciplinary point of view. Fortunately, several initiatives are currently underway and others are pending evaluation:

-ARTOG-Bern. Urogenital Engineering (Swiss National Science Foundation). UGE is part of the ENIUS COST Action and has well-established collaborations with the major research groups in the field.

- Proposal: 101072813 — EURETHRA. Call: HORIZON-MSCA-2021-DN-01. Marie Skłodowska-Curie Actions & Support to Experts A.1 – MSCA Doctoral Networks. Main proposer. Dr. Petra de Graaft. EURETHRA sets out to construct a Doctoral Network to train doctoral candidates in the field of urinary regenerative medicine who can fill this knowledge gap. With a strong and interdisciplinary consortium consisting of 17 academic and industrial experts in (re)generation of the urethra, we will set up an interdisciplinary European training programme covering regenerative medicine techniques, clinical disease models, and

development and commercialisation of innovative technologies for biomaterials and tissue engineering.

-Call: HORIZON-CL4-2022-RESILIENCE-01. Proposal number: 101091814. Proposal acronym: “Hydrumetal. A metal-based biodegradable ureteral stent”. Hydrumetal will develop an innovative implantable medical device biodegradable ureteral stent for long-term applications composed of new smart and multifunctional biomaterials-, biodegradable alloys coated with a smart and multifunctional hydrogel, to be used in surgical domain.
-COST INNOVATORS GRANT APPLICATION. CA16217, February, 2022. “Urinary stents and catheters from bench to bedside software·. Under evaluation.
- InVivo Bionics (Norway). Ingelin Clausen (MC member, Norway).
-Urinary stents. Current state and future perspectives. F. Soria, D. Rako. P. de Graaft editors. OA Springer Nature, 2022.

Capacity-building objectives

Objective 6. **To consolidate a multidisciplinary network actively involved in urinary stents research to facilitate scientific knowledge exchange through, Workshops, TS, scientific papers, and guidelines.**

Since the Kick off Meeting, we have carried out 17 activities including TS, Workshops and conferences. Five of them were online, and in spite of their online presentation format, the results were very positive. That is the reason because our last ENIUS Workshop (tomorrow), we have held the in a hybrid format (face to face and online). Venues: Porto (Portugal) Workshop-2018; Oxford (UK) TS-2018; Cáceres (Spain) TS-2018; Sofia (Bulgaria) Workshop-2019, Sofia (Bulgaria) WGs-Workshop-2019; La Valleta (Malta) Workshop-2019; Bern (Switzerland) TS-2019, Lublin (Poland) TS-2019; Belgrade (Serbia) Workshop-2020, Belgrade (Serbia) WGs-Workshop-2020; I Virtual Workshop-WG4-5-2021; Virtual Conference-WG1-2021; Virtual Conference-WG2-2021; Virtual Conference-WG4-5-2021; II Virtual Workshop-WG6-2021; Istanbul-(Turkey) Workshop-2022. We reached up to 594 participants in our Workshops and TS. The number of members of our COST Action was 207. 15 scientific manuscripts and a book focusing on urinary stents and future lines of research have been published.
One of the greatest achievements of this network is the enormous cohesion and multidisciplinary nature of its members, which has favoured the achievement of the proposed objectives and will allow a multitude of advances in the area of urinary stents and biomaterials to emerge from this network.

Objective 7. To create a cohort of skilled bioengineer/researchers with experience in stents by providing TS and supporting Exchange visits between Research Centres.

Young researchers have performed 77.7% of our STSMs, hold 46.6% of leadership positions, and have been invited as speakers in 47% of our network's training activities. They make up 79.6% of the attendees at our training activities. This gives an idea of the great involvement that our network has had with young researchers and the important impact it has had on their training. The assessment of ENIUS' lifetime in this area can be summarised as follows: In our MoU we had a forecast of 16 STSMs and finally up to 28 STSMs have been carried out, which is a great pleasure for this network. This has been one of the activities most in demand due to the large number of centres that make up ENIUS and the importance of establishing relations between the different research groups. The participation of a very high percentage of young researchers has led to our expectations being exceeded.

Objective 8. This COST Action will play a seminal role in facilitating links within researchers and industrial communities. A transfer of technological knowledge to the industry will foster industrial competitiveness of Europe.
Over the duration of our multidisciplinary network we have been able to contact and have up to 10 companies as well as one stakeholder (U-Merge. Urology in emerging countries) become part of our network: Cook Medical; Boston Scientific; Teleflex; Pnn Medical; Devicare; Coloplast; AlviMedica; Taewoong Medical; U-Merge; HydruStent; Invivo Bionics AS. Members of the industrial community have actively involved in a multitude of activities, mainly TS and Workshops, which have allowed for closer relationships between researchers and members of the urinary stent and biomaterials industry. Some of these relationships are reflected in project proposals, as well as in the partnership for the development of urological medical devices.

ENIUS NETWORK SUCCESSES

The main achievement is to have managed to bring together in a single group the large number of research groups and companies working in the development of urinary stents. The multidisciplinary character of this group is its main strength and the important representation of leading groups in their areas has been a great success. To be able to count on a network that has been cohesive over the years and that has understood the need we have for each other is an important achievement. It has been realised that there was a need for such a network, which could bring together all stakeholders in this area, as the strengths of some can reduce the weaknesses of other groups. This can put an end to the isolation of many groups and will obviously lead to further scientific and technological progress in stents, which has a direct impact on patients and the industrial fabric. There is a common understanding that our strength has been the multidisciplinary network and that this network has made us all stronger to achieve our goals.

Another important achievement of this COST Action has been the important group of young researchers who have had the opportunity to be part of the network. They have benefited in their training as researchers, through their participation as students and as speakers, the large number of STSMs they have carried out (76% of STSM applicants have been young researchers), as well as in learning leadership positions in research networks. Many young researcher-led papers have been produced and our activities have always required young people to present their research work, to help them in their training. Consequently, we have collaborated to create a cohort of researchers in a research area with a small number of researchers, which will facilitate future results contributing to the improvement of urinary stents.

Dr. Federico Soria
ENIUS Action Chair.