European Metrology
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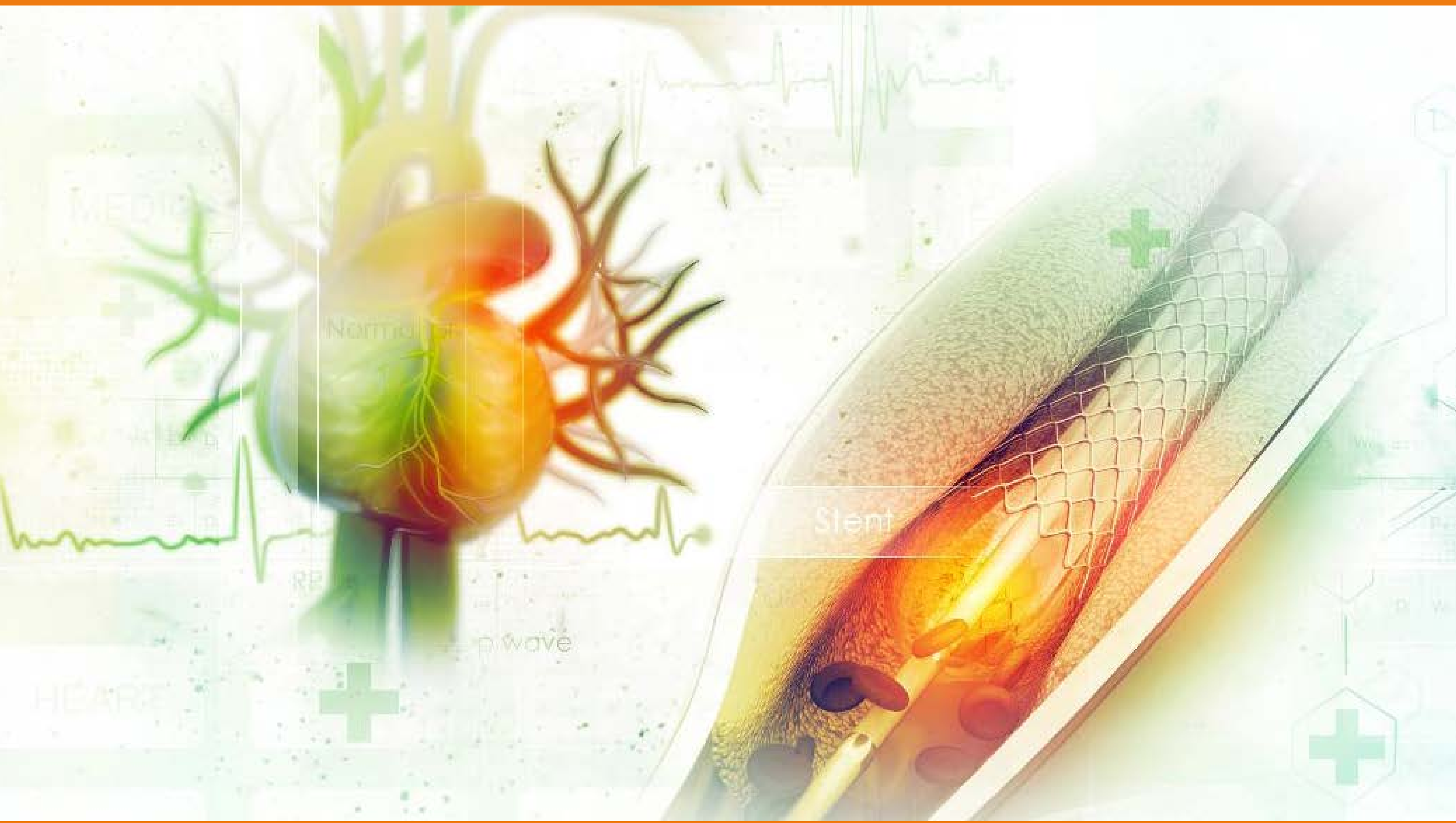
EURAMET



Precision for complex drug layers

Manufacturing complex layered structures, for example drug delivery mechanisms on medical implants, relies on chemical interactions to deliver functionality. Advanced analysis methods confirm chemical layer performance at all stages of the production process from research through to confirming the quality of finished products. Complex functional layers are used in long-term medical implants but to optimise patient outcomes greater accuracy for analysis methods is needed.

Europe's National Measurement Institutes working together

The European Metrology Research Programme (EMRP) brings together National Measurement Institutes in 23 countries to address key measurement challenges at a European level. It supports collaborative research to ensure that measurement science meets the future needs of industry and wider society.

Challenge

Films and coatings with complex layers often introduce formidable surface chemistry challenges in advanced manufacturing processes, such as constructing electronics based on non-silicon semiconductors or in drug delivering layers used in medical implants. Biochemical surface interactions have particular importance for patient wellbeing during surgery and afterwards while the body acclimatises to a new implanted device.

To avoid rejection of an implant, its surface layers are designed to release anti-inflammatory and antibiotic drugs over time. Precise control of its near surface chemistry is essential to ensure the reliability and effectiveness of drug delivery. Manufacturers are looking for exact methods that will reliably map surface layers in 2-D and 3-D to obtain a better understanding of how drugs are distributed in implant layers. With this knowledge devising optimised drug layer release rates will offer them the potential to tailor implants to individual patient requirements. A first step towards this goal is improving the accuracy of measurements made using advanced analytical instruments. This requires the development of robust reference materials that match both the types of chemicals and substrates used in implants to confirm instrument performance.

Solution

The EMRP Project, *Chemical metrology tools to support the manufacture of advanced biomaterials in the medical device industry,* investigated the use of a range of high vacuum analytical techniques including Time of Flight Secondary Ion Mass Spectrometry (ToF SIMS) to characterise chemical layers used in medical device manufacture. This technique is based on the removal of thin layers from a coating surface using a focused analytical ion beam followed by mass spectrometry analysis to accurately determine how chemical layers change with depth below the materials surface.

Samples of flat implant materials were carefully prepared with known chemical properties and these were used to characterise the task specific measurement capabilities of the Tof SIMS technique in the project. Once the team were confident that results matched the samples known chemistry, the technique was extended to the more complex geometries of real world medical devices.

Impact

B. Braun Melsungen AG is a leading manufacturer of a wide range of healthcare products worldwide, including stents used to support and widen narrowed arteries in patients. Some 2.2.million stents are used globally every year in surgical procedures. These consist of a wire mesh coated with thin layers of anti-inflammatory and antibacterial drugs to ensure improved patient acceptance of these life saving devices. Optimising drug delivery directly into coronary arteries is now a possibility thanks to the project's new Tof SIMS method.

B.Braun are keen to use the new Tof SIMS capability in research on how drug concentrations can be varied with depth in stent chemical layers to enable the rapid release of higher concentrations immediately after implantation with amounts reducing over time as the body adapts to the implant. This opens the possibility for developing the next generation of arterial stents with drug layers tailored to individual patient requirements. Greater accuracy in determining the chemical composition of surface layers will contribute to increased European competiveness in the global medical device market estimated to be worth 70 billion euro to the EU economy annually.

Chemical tools support medical industry

The EMRP project *Chemical metrology tools to support the manufacture of advanced biomaterials in the medical device industry,* developed new high-vacuum analytical tools for accurately characterising thin films and surface implants coatings, and investigated optical techniques such as vibrational spectroscopy for potential application in surgical implant manufacturing environments. This project has had an immediate and lasting impact on the global competitiveness of the European medical implant industry by providing a suite of advanced analytical techniques validated using appropriate reference materials derived from real medical devices. Using the project's analytical techniques has enabled the development of new medical devices, such as urinary catheters with novel coatings, prostheses with improved performance, and improved assessments of implant corrosion.

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