A whole new dimension of imaging precision

By Julia Maciejek, DTI

Like many fields in dentistry, implantology has been formed by technological innovations since its humble beginnings more than half a century ago. As the aesthetic and osseointegration properties of implant materials have continued to improve, the number of dental patients opting for implants has risen steadily. With this increase in procedures has come a demand for atraumatic and safe surgery with fewer postoperative complications. Since 2005, French company ACTEON has established itself as a leader in digital medical imaging and high-frequency ultrasonic devices. Supported by its excellent clinical results, ACTEON continues to push the boundaries of what is possible in implantology as it seeks to provide products that optimise both the patient’s and the dentist’s experience.

With an emphasis on research and development in dentistry and medicine, ACTEON has successfully expanded its offering and introduced new products earlier this year. Its two multidisciplinary research and development teams and four manufacturing plants are all located in western Europe: in Mérignac (equipment and pharmaceutical) and La Ciotat in France (dental imaging), Tutlingen in Germany (medical imaging) and Milan in Italy (dental imaging). These teams work very closely together and production processes are highly controlled owing to their geographical proximity. This is further enhanced through collaboration with international dental surgeons, leading to the manufacture of devices that, according to ACTEON, deliver the best results for patients through minimally invasive and less traumatic treatments.

ACTEON granted Dental Tribune International an exclusive look behind the scenes of its 5,300m² manufacturing plant in Milan, where many of the company’s introral and extraoral imaging devices are produced. The team was proud to introduce its flagship model: X-Mind trium. This extraoral radiographic unit was first introduced at the International Dental Show (IDS) in 2015 and received a major update just in time for the 2017 fair. It offers a complete range of innovative solutions for diagnostics and treatment planning. Considerable attention has been paid to image quality and homogeneity, including X-ray emission, processing, stability and geometry. “X-Mind trium combines CBCT, panoramic and cephalometric imaging, which is why it is called a three-in-one device,” explained Claudio Giani, director of imaging research and development at the Milan site. He demonstrated that CBCT imaging is accomplished using a rotating gantry with a fixed X-ray source and a detector. Giani told us that, during the rotation, multiple sequential projection images, ranging from 150 to 450, are acquired to complete the arc. This procedure varies from a conventional medical CT scan, which uses a fan-shaped X-ray beam in a helical progression to acquire individual image slices of the field of view (FOV) and then stacks the slices to obtain a 3-D representation.

When we first approached X-Mind trium, we noticed right away the distinctive ergonomics of the radiographic unit. The device has an extremely short U-arm, which moves around the patient during the image acquisition phase. This is supported by the patient’s kinematics and collimation and aids comfortable positioning of the patient’s jaw. The entire system is designed with ergonomic efficiency in mind and takes up very little space in the practice room. With a secondary collimator (X-ray tube assembly) installed, the patient is not exposed to additional collimator movements.

Excellent quality assurance

ACTEON produces high-end quality products that undergo a tried-and-tested quality control process. “The production of X-Mind trium has risen month after month, especially since we obtained U.S. Food and Drug Administration approval and then launched X-Mind trium in the U.S. stated Alvise Reither, the Milan factory manager. He explained that, by changing the factory’s layout and the flow of materials, new workflow processes were established. The manufacturing plant is continuously expanding, and with additional operators, it is able to meet the demands of the market. “In this factory, we use the Kanban approach principle, which means that we produce on stock, but finalise the product based on order. This way, we can balance demand with available capacity,” added Reither.

Moreover, ACTEON applies significant quality controls during all processes, from the assembly of the core of the machine to final testing, which includes checking of the components and the configuration of the workstation. According to the factory manager, this procedure has been streamlined significantly in comparison to last year. Reither showed us a large number of testing cabinets containing devices being checked. With complete concentration, employees in front of computers verify the correctness of every step before the X-Mind trium units are distributed. It is in this context that a large quantity of X-Mind trium devices are manufactured, tested and shipped each week.

“We have an excellent product quality. We want to ensure a high-quality standard, so employees take turns at the workstations. We also want to make sure that each employer knows and understands all the processes leading up to the finalisation of the product, establishing an appreciation of the importance of each step in the assembly. We further want our employees to respect ACTEON’s standard of quality. This follows the two steps of the quality control. (1) checking that all cables and parts are well assembled and (2) testing the machine’s functionality in the testing cabinets. Our quality manager also inspects the components when they are sent to us and before we put them into stock. No parts are assembled externally. A mix of components, cables, mechanical parts, motors and sensors are assembled. That is also part of our quality management.” Reither detailed.

Sharp images

Excellent image quality is essential for treatment planning and diagnosis. In CBCT, exposure is incorporated in the FOV. This means that only one rotational sequence of the gantry is necessary to acquire enough data for image reconstruction. “In implantology, a CBCT image is indispensable for planning simulation and determining the exact nerve location. With only one image, the entire dental arch can be visualised, which allows for optimal diagnostic planning possibilities. X-Mind trium has a range of FOV options displayed in detail and without movement artefacts. He emphasised that the exposure time is very low and the reconstruction time is three seconds. We saw that, with a cephalometric image, the entire maxillofacial area is shown, making it highly suitable for oral and maxillofacial surgeons. Furthermore, it has a small voxel size of only 75µm and a fast construction time of 29 seconds. X-Mind trium can be equipped with one or two sensors for an efficient workflow.

With ACTEON’s expertise in medical imaging, a dedicated analytical algorithm has been implemented for X-Mind trium. “We have achieved exceptional results, which are able to provide advanced clinical indicators that will be helpful for practitioners in the future,” stated Giani proudly. “The analytical algorithm has been developed in terms of the graphics processing unit (GPU) and a specific type of GPU is installed inside the workstation of X-Mind trium when the CBCT function is configured,” explained Giani.

This algorithm is used to determine the apparent image definition and bone density to facilitate clinical decision-making. The filters ensure detailed recording of the imaging acquisition by low-noise micro-stepping motors.

Low radiation dose

With X-Mind trium, high radiation exposure is a thing of the past. The low-radiation protocol decreases the required amount of X-ray emissions by a third using the algebraic reconstruction technique. This means that the radiation dose for the patient can be reduced by 50 to 70 per cent. This low-dose imaging guarantees a maximum FOV with minimal radiation exposure to the patient. “This is essential because we do not care only about good images but also about the well-being of the patients,” stated Reither. Furthermore, the software of X-Mind trium monitors radia-
tion and ensures that the levels of exposure are kept low.

User-friendly software

Computer scientists would say the software is as important as the hardware. ACTEON provides intuitive and ergonomic imaging software that has all the required functions—scanning, measuring, editing, commenting. In the factory cellar, Reither explained the special features of the ACTEON Imaging Suite software and stated that it can be linked to most practice management software and all ACTEON imaging products, such as the X-Mind trium, CBCT and panoramic devices, and intraoral scanners. It is compatible with both macOs (and soon iOs) and Windows and has a TWAIN driver for full compatibility with all imaging software. This gives practitioners the ability to move around and interact directly with their patients.

The radiographic unit is in continual operation at most dental practices. It is clearly imperative then to ensure that dental professionals have the skills to adequately handle the devices and take high-quality images with the correct settings. “The user-friendly software enables the customer to either use the workstation provided or use their own. However, with the workstation provided, our professional and efficient team of service technicians can perform remote connections to solve problems of configuration or calibration. We want our customers to choose the software option that is best for them,” explained Reither.

Safe surgery

X-Mind trium offers extraordinary functionality in the field of implantology, making it suitable for more demanding treatments. Misleading or insufficient information obtained from a radiograph can lead to the loss of an implant, one of the worst scenarios for both the patient and the dentist. “In pre-implant procedures, accurate measurements of the bone density and volume are essential to guarantee a higher success rate in implantology. The 3-D capability of X-Mind trium also facilitates safer osseointegration,” said Giani. Clinical decision-making has seemingly become easier than ever with X-Mind trium.

Certainly, our tour would not have been complete without a look at ACTEON’s well-known Piezotome ultrasonic brand. Thousands of dentists worldwide have adopted the company’s celebrated Piezotome devices as their choice for pre-implant surgery, with Piezotome Cube representing ACTEON’s new standard. It is a powerful ultrasonic device with a rotary motor, as well as a handpiece and a tip, ensuring optimum performance. Leading oral surgeon and implantologist Dr Angelo Trodhan successfully uses Piezotome Cube in his everyday treatment procedures. “The Piezotome’s ergonomics makes the device naturally intuitive and reliable. Furthermore, it enables surgeons with less experience to perform a variety of treatments. In accordance with the cutting selectivity, soft tissue (membranes and nerves) is preserved. During piezoelectric surgery, fine and precise cuts minimise bone loss. In 98 per cent of cases, patients do not need to use analgesics postoperatively and barely any swelling is observed. Surgery with Piezotome Cube maintains the patient’s quality of life,” said Trodhan.

In implantology, bone grafting materials may be necessary for the implant to succeed. For this reason, QUALIOS was developed, and it was first introduced at IDS 2017. The material has a unique bone-supporting structure and high level of mechanical resistance. Its large interconnected pores make it particularly suited to bone colonisation, and it is completely resorbable, ensuring high-quality bone regeneration. Being entirely synthetic, it is free of any contamination risk that comes with products of animal or human origin. It is clear from this that QUALIOS complements ACTEON’s implantology product line.

In ACTEON’s continuous product expansion, patients’ well-being continues to be the top priority. We felt the passion employees put into their daily work to support ACTEON’s innovative portfolio for imaging and piezoelectric surgery. These products have positioned the company as a pioneer in oral surgery and dentistry. They are less invasive, safer and faster to operate, and provide patients and practitioners with the best treatment options available.
With Trefoil, Nobel Biocare recently introduced a new implant solution or protocol for achieving a fixed, definitive fixed full-arch restoration of the mandible in one day. Combining a pre-manufactured titanium bar, three implants and a simplified restorative workflow without provisions, it reduces the time to teeth and chair time compared with conventional fixed treatment with implants, according to the company.

At its recently held London symposium, Dental Tribune spoke with oral and maxillofacial surgeon Dr Rubén Davó from Alicante in Spain, about the system.

You were one of the first clinicians worldwide to have worked with Trefoil and evaluated its clinical performance. How did you become involved, and what results have you achieved?

I have been collaborating with Nobel Biocare’s clinical research department for many years on various projects. Nevertheless, it was an honour and privilege when they asked me to clinically evaluate the new Trefoil system. From a surgical point of view, we looked at the accuracy of the template guided surgery. We know that the fixation-compensation mechanism allows around 0.5 mm of discrepancy. In our clinical study, we found that structures could be placed properly in more than 99 per cent of the cases.

Almost 20 years ago, a similar treatment protocol was introduced to the market with Bränemark Novum, but it was discontinued in 2007. What makes the Trefoil system different?

In my opinion, the Brånemark Novum system was ahead of its time. While from a clinical point of view it demonstrated good success rates, the market was not ready for it. You have to remember that, in those days, treatment concepts like immediate loading or guided surgery did not exist. Furthermore, usually a high number of implants were used to rehabilitate edentulous patients.

However, the main problems with Novum were related to the prosthetic framework, which posed difficulties from a functional and aesthetic standpoint. As a refined system, Trefoil has completely addressed these problems.

What patient groups are going to benefit from this new protocol?

Potentially all patients edentulous or soon-to-be edentulous because this protocol does not depend on new technologies or sophisticated therapies. It requires only one surgeon and a basic laboratory to provide patients with fixed immediate teeth.

How difficult is it to learn the Trefoil protocol?

I would recommend doing at least five cases. After that, the clinician should feel comfortable and confident in performing the protocol. While it is not a very complex surgery, the practitioner will need a little bit of training. Nobel Biocare is very aware of that and offers a number of courses in many markets.

You have led some of these courses in Germany, Spain and the UK, to name a few. What has the initial feedback been?

Those who were involved in the clinical studies on Trefoil are teaching the courses now, and this has the advantage that attendees can gain from our experience gained in treating many of these cases. Our goal is to avoid both complications and any possible problems. The feedback has been extremely positive. Many participants have taken the course because they felt it offered the right concepts and provided a good practical learning experience. Consequently, they felt very comfortable performing the surgery.

According to Dr Kenji W. Higuchi, one of the developers of Trefoil, the system will be the next big thing in implant dentistry. Would you agree with that statement?

I think it has become very difficult to innovate in this field because many things have been introduced over the last 20 years. I have no doubt however that, in China, India and other developing countries, this will start a revolution because now more people will have access to these treatment possibilities. Trefoil will also address a gap in many Western countries, where we see many patients that do not want removable dentures, but cannot afford fixed dentures because of a lack of time or money. However, all the positive feedback we have received lately has made us extremely positive about the future prospects of the system.

Thank you very much for the interview.
Dental biofilms play a crucial role in the overall health of the oral cavity. They are composed of bacteria, bacterial products, extracellular DNA and extracellular matrix that serves to bind biofilm together and contributes to the characteristic stickiness of plaque. As a complex ecological community on hard surfaces of the dentition, such as teeth, they produce virulence compounds that exacerbate the host inflammatory response.

Plaque bacteria utilise nutrients from saliva and the food we eat for their energy needs and metabolic requirements. Interventions, which employ a combination of actives and attributes unique to each product, include the use of tooth-brushes, mouthrinses, toothpastes and chewing gum, which take advantage of salivary flow and mastication mechanics unique to the oral cavity.

Optimising interventions against biofilm requires a thorough understanding of its dynamics and physical characteristics. In the case of actives present in tooth-pastes, mouthrinses or chewing gum, this knowledge provides the foundation for understanding how effect biofilms and affects bacterial metabolic pathways to reduce overall activity.

Ultrastructural invasive techniques such as fluorescence in situ hybridisation have been useful in visualising the location of labelled bacteria in oral biofilm samples. In some cases, select biofilm metabolites have been fluorescently tagged and traced in the biofilm, but they remain invasive techniques requiring considerable sample preparation. Clearly, new technologies that provide a more global, comprehensive and real-time assessment of what is truly taking place in the multispecies biofilm are needed.

A novel technology known as “laser ablation electrospray ionisation for mass spectrometry” (LAESI-MS) has revolutionised sample introduction and data analysis for high-throughput biological MS. The LAESI-DP-1000 system (Protea Biosciences) is a new-generation high-throughput direct ionisation system that directly analyses biological samples containing water without the need to apply chemicals or introduce tags or tracers, thus allowing for virtually no sample preparation.

Most significantly, the technology performs 2- and 3-D depth profiling of oral biofilms, allowing for analysis of the 3-D spatial distribution of various molecules throughout the biofilm directly as they exist in nature. This study investigates both the distribution and the effect of a test active on select molecules and metabolites in oral biofilms to assess its antimicrobial or antiplaque effects.

The experimental protocol

In order to simulate the topography, growth conditions and substratum on which dental biofilm grows, pooled human saliva was used to grow two-day mixed species biofilms on horizontally suspended hydroxyapatite (HA) discs. Prior to inoculation by multispecies bacteria, the discs were pretreated with filtered pooled saliva to allow for the proteins that enable initial bacterial attachment to coat the discs. This step is known as “preconditioning.” Inoculum was then added together with 100 ppm of the test active to monitor effects on adherence and colonisation of biofilm bacteria in the substrate.

Additional multispecies saliva biofilms were generated using no-treatment controls. Untreated and treated biofilms were then frozen at −80°C to ensure preservation of the biofilm architecture prior to LAESI analysis. LAESI-MS and tandem MS were applied to determine the 3-D spatial distribution of the active and the various molecules the active potentially affected in the myriad metabolic and chemical signalling pathways of the biofilm. These molecules included quorum sensing factors, metabolites, virulence factors, and others. The area of analysis for both the untreated and the active-treated biofilms on HA discs is shown in Figure 2.

Results

As mentioned earlier, the spatial distribution of the active in the experimentally treated biofilms was assessable in both 2- and 3-D. Heat map analysis of three horizontal planes with their corresponding x and y coordinates provided precise localisation of the active for each plane in the untreated and treated biofilms. The composite result of the vertically stacked heat maps allowed for relative localisation of the active in the treated sample for each of the five planes, revealing the highest concentration in the plane furthest from the substratum (Fig. 3).

In addition to mapping where any given active had penetrated the oral biofilm, LAESI was used to map relative localisation of select molecules in the treated and untreated biofilms. The autoin- ducer-2 chemical signalling molecule, which is involved in cell density-dependent quorum sensing, was mapped. The heat map signal for this molecule was considerably reduced throughout all coordinates, relative to untreated controls, indicating reduction of the presence and activity of this molecule and thus suggesting that the active reduced levels of autoinducer-2 in the treated biofilms.

In addition, the levels of the amino acids arginine and lysine were investigated in untreated and treated biofilms. Arginine is naturally found in saliva and is utilised by some plaque bacteria, resulting in the production of ammonia and carbon dioxide. These two amino acids were chosen as surrogate molecules to further validate the use of LAESI to map diverse molecules of interest in the oral biofilm. Arginine was found in greater abundance relative to lysine in the untreated...
samples, as shown in their respective heat map analyses. Upon treatment with the active, the levels of both molecules were drastically reduced relative to their untreated controls.

Finally, the levels of lactate were investigated in untreated and treated biofilms. Lactate is a by-product of sugar fermentation by caries-causing bacteria such as *Streptococcus mutans*, which converts sucrose to the sticky glucans that help keep the biofilm intact. Thus, the relative levels of lactate can serve as an indicator of cariogenic activity or the risk of caries progression in the supragingival plaque biofilm. Comparison of the heat maps of the untreated biofilms to those of the active-treated biofilms showed relative reduction of lactate levels in the treated biofilms for all $x$ and $y$ coordinates investigated (Figs. 4a–d).

Discussion and future implications

The application of an MS-based analytical method for oral biofilms that requires virtually no sample preparation represents a breakthrough in improving our understanding of what is really taking place in the oral plaque biofilm in response to chemical challenges. Mere removal of bulk plaque biomass from the interproximal sites is insufficient to account for paradoxical clinical outcomes of test subjects whose gingival health improved even when little plaque biomass was removed. This suggests that the biological activity of specific plaque toxins and other bacterial products embedded in plaque biofilms and their distribution in the biofilm may be more important in triggering the gingival inflammatory response than bulk plaque alone. It is important to understand where these bacterial compounds or metabolic by-products localise in the plaque biofilm, since their location can influence both the magnitude and the sustainability of the pathogenic response.

Pathogenicity factors that localise closer to the biofilm–substratum interface may prove to be better protected from external chemical or mechanical stressors. In instances in which the compound adversely affects the sub- stratum itself (such as lactate and its role in demineralising HA), the continued close proximity of the compound to vulnerable substratum may prove to be particularly harmful over time. Being able to construct a stratified map of where these compounds localise in the layers of the biofilm thus provides strategic insights into how to best manage them.

Conversely, there is little knowledge to date, but high value gained, in understanding how chemical actives directed against the biofilm and its constituents behave as a function of how deeply the actives penetrate the oral biofilm. Although antiplaque efficacy can be gauged as antiplaque (e.g. destabilising or disaggregating biofilm), antimicrobial (e.g. bacteria-killing) or a combination of both effects, it is clear that multiple factors that act in concert to constrain the biofilm penetration capacity of many actives found in toothpastes, mouthrinses and medicated chewing gums will ultimately reduce antiplaque efficacy of even the most effective chemistries.

Ultimately, developments such as quantitative measurement of biofilm depth from the underlying substratum to the surface of the biofilm, along with co-localisation and quantification of levels of actives relative to the concentration of surrounding molecules of interest, will bridge the gaps in establishing a direct causal relationship between the active and the metabolic pathways it affects. The reported investigation represents the first successful demonstration of this application in dental research.

It is envisioned that future research interests will also be expanded into analysis of biofilm on coupons grown in the human mouth to generate plaque biofilms truly grown in the oral cavity that can be conveniently removed and later analysed ex situ. This will inform transient changes in crucial metabolic pathways in naturally occurring plaque and may help identify predictable markers for charting plaque regrowth after external challenges. LAESI thus represents a unique tool for exploring the inner workings of oral plaque biofilms that combines the sensitivity of MS analytical chemistry, the 3-D visual analysis afforded by confocal microscopy and minimal effort in sample preparation.