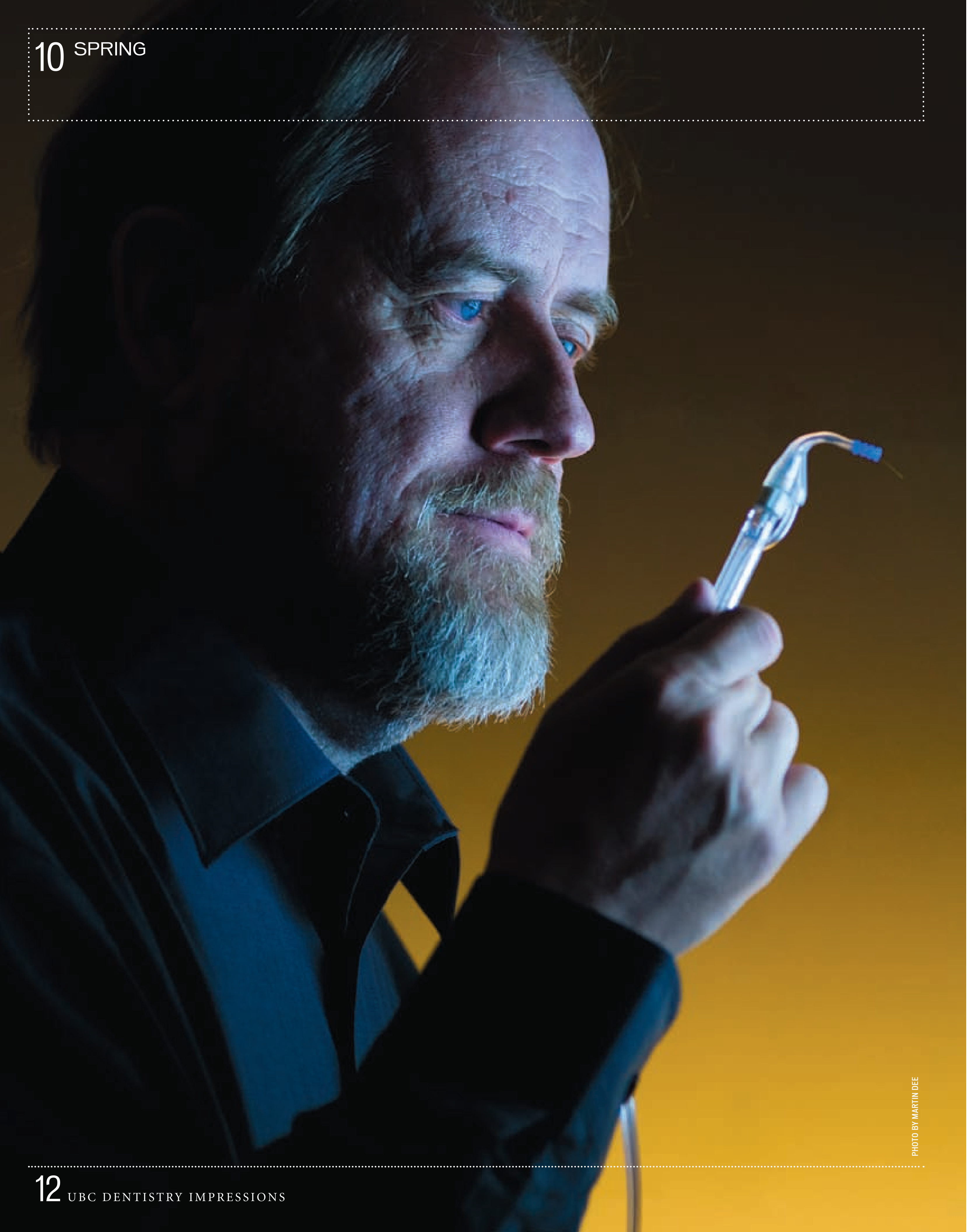
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BATTLING BIOFILMS–INNOVATIONS IN ENDODONTICS

BY MARI-LOU ROWLEY

Computational fluid dynamics, multimedia teaching tools and novel irrigation fluids are among the arsenal of technologies developed and employed by UBC Dentistry professor Markus Haapasalo. They are all part of a multiple attack strategy to eradicate biofilms—pernicious colonies of bacteria that destroy teeth, roots and gums.

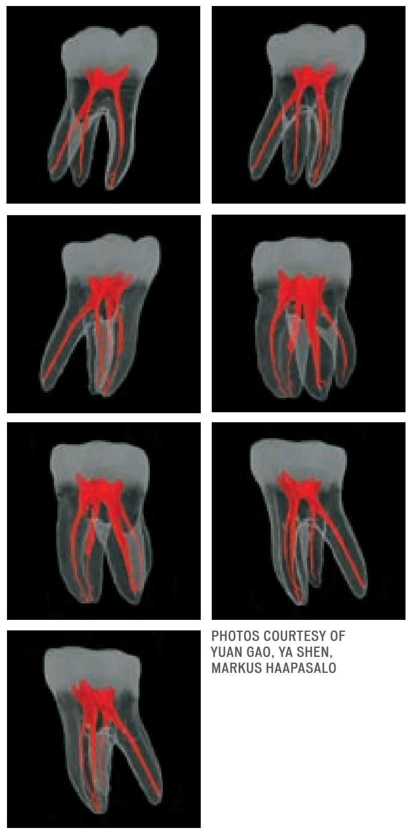
In the long history of dentistry, endodontics—the treatment of diseases of the tooth root and pulp—is a relatively new specialty, recognized by the American Dental Association in 1963. Prior to modern root canal procedures, treatment was often extraction and dentures. Despite advances in procedures, however, 30 to 50 percent of the root canal surface area in many teeth isn't amenable to mechanical cleaning. It is too difficult to reach all areas of the canal crevices, and the bacteria that lurk in them are too pernicious. In addition, up to 90 percent of endodontic disease is asymptomatic until it reaches the crisis point—a throbbing toothache.

At the peak of his career, and at the age of 50, endodontist Markus Haapasalo came to UBC from Oslo to undertake clinical research that is upping the odds for positive patient outcomes, while reducing pain and discomfort and revamping the image of endodontics for the root canal–phobic. "There have been remarkable changes in the field of endodontics in the past 10 years, resulting in a shift away from mechanically focused treatment to a more biological approach," notes Haapasalo. "I regard endodontics—and dentistry in general—as just one specialty in the field of medicine, of which research is an integral part."

In collaboration with clinician researchers and industry partners around the world, Haapasalo is at the forefront of this sea-change. Tidal metaphors are apt for what he does. Root canal systems resemble complex, microscopic irrigation channels. If bacteria get into the system and cause disease of the pulp, or root interior that houses the nerves, the circulation in the root is permanently destroyed. Without blood flow, the body's defence system can't mount a response, and the tooth dies.

"This is just one reason why we don't use systemic antibiotics to treat root canal infection, since antibiotics need to circulate in the bloodstream to be effective," he explains.

Another reason why antibiotics don't work is that the life cycle of biofilms is relatively slow, with bacteria multiplying roughly once per week. In contrast, most antibiotics were developed to kill bacteria grown under optimal conditions, where multiplication occurs once every 20 minutes. In the slower ecosystem of biofilms, antibiotics are just not effective.



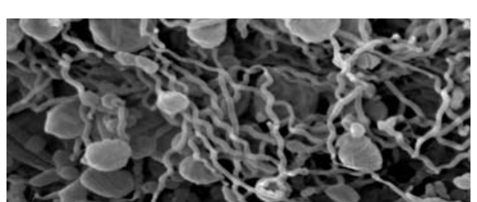
PHOTOS COURTESY OF YUAN GAO, YA SHEN, MARKUS HAAPASALO

Using Technology to Thwart Biofilms

Perhaps the most challenging aspect of treating root canal infections lies in the ubiquitous nature of bacterial biofilms themselves. Unlike a single species bacterium that might be responsible for a throat or respiratory infection, most bacteria form in colonies known as biofilms. And like most living systems, biofilms need something to "hang on" to. The thin pink films that form at the bottom of a water jug, in the basin of a humidifier or on a mouthguard are common examples of biofilms. They consist of numerous types of bacteria that coexist in their own unique ecosystem—a cocktail of morphotypes intertwined and interdependent. Under the microscope biofilms may look beautiful, but they wreak havoc with biological and even industrial systems.

"These bacteria all have specific functions within their 'bacterial society,'" says Haapasalo. "Even in non-endodontic environments, antibiotics can be ineffective because there are so many different species of bacteria, and some have enzymes that destroy the action of the drug."

Haapasalo and his research team simulate an actual in vivo root canal system and build biofilm colonies in vitro, in the laboratory setting. Using powerful confocal laser scanning microscopy (CLSM), they are able to obtain detailed images of biofilm structure for analysis. In a recently published study, Haapasalo and his group were the first to create multispecies biofilms in vitro that closely simulate oral in vivo multispecies biofilms. In particular, they were the first group to successfully cultivate biofilm with an abundant growth of corkscrew-shaped spirochete bacteria (see illustration below).



An abundant growth of corkscrew-shaped spirochete bacteria.

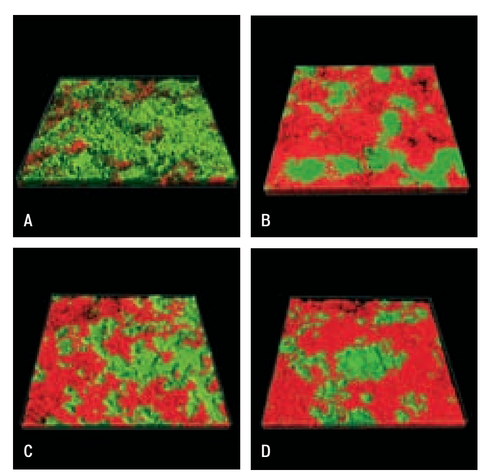
PHOTO COURTESY OF YA SHEN, MARKUS HAAPASALO, WEI QIAN

Irrigation Key to Root Canal Treatment

The shift towards a biological approach to treating root canal disease lies in irrigation of the canal system in order to maximize the effectiveness of disinfection. "This is the important strategic or philosophical difference," notes Haapasalo. "We now understand that the main benefit from instrumentation is to make effective irrigation physically possible."

Dental irrigants are chemical fluids that dissolve infected pulp tissue and attack bacteria. With support from industry, including Vista Dental and Dentsply among others, Haapasalo's group studied the effectiveness of different irrigants against biofilms grown in his laboratory. They helped to improve the effectiveness of the irrigating solutions in tissue dissolution and against biofilm bacteria (see illustration, figures A to D). "Our research is both basic and translational, which makes it natural that we have active collaboration with industry," Haapasalo says.

While traditional approaches use irrigants with a single active component, Haapasalo is working to develop a multi-agent approach that attacks different aspects of bacterial cell membranes. His group has recently patented a novel irrigation fluid with UBC's Industry Liaison Office.



PHOTOS COURTESY OF YA SHEN

Biofilm treated with 2% CHX treatment for 3 min (A); CHX-Plus treatment for 3 min (B); 2% treatment for 10 min (C); CHX-Plus treatment for 10 min (D). Green (viable cells); red (dead cells).

Root Canal Fluid Dynamics

Computational fluid dynamics is an area of research usually associated with large-scale phenomena and related problems, such as forecasting weather, developing drilling mud and managing hydroelectric systems. But fluid flow problems exist at the microscopic level of the root canal systems as well. The velocity, distribution, volume and pressure of irrigants, the root canal shape and size, and the type, size and insertion depth of needles all complicate the endodontist's task. In addition, the complexity of root canal anatomy makes it difficult to observe how effectively irrigants flush through the system.

"The hydrodynamics of the root canal are very different than in macro environments, such as a dam on a river for instance, because the 'banks' in a root canal system are so close together," Haapasalo explains.

In an international collaboration with colleagues at UBC and in China, Haapasalo developed a 3D computational fluid dynamic model of root canal irrigation. By testing their virtual model with different mathematical algorithms, and then comparing the results with a standardized fabricated model, they were able to validate their model against what happens in a physical setting.

"Now that we have found the right algorithm, we can start to study in detail how to optimize the physics of irrigation for effectiveness and safety," he says. It is a delicate balance; under-irrigation can leave traces of bacteria, while over-irrigation can cause tissue damage and even pain.

In addition, when someone has an unusually shaped root canal, the instrumentation may not be able to reach into the root. Haapasalo is also developing the first flexible ultrasound needle tip for root canal irrigation. The benefit would be to reach more difficult configurations and to maximize spreading of the irrigant using ultrasound vibrations.

"Eradication of dental biofilm requires multiple attack strategies," says Haapasalo. "Today, there is a whole new philosophy for cleaning and disinfection of the root canal that is completely different from traditional approaches, and we are working together with industry to develop many novel techniques."

PHOTO BY MARTIN DEE

Expanding Teaching and Learning

A native of Finland, Dr. Haapasalo came to UBC from Oslo in 2004, after two previous visits and fruitful collaborations with former Science dean Dr. Barry McBride. Haapasalo's reputation preceded him, and he continues to play a very active role in international scholarship and teaching. He is editor-in-chief of *Endodontic Topics*, and the first non-US associate editor of the *Journal of Endodontics*.

Haapasalo was instrumental in establishing UBC Dentistry's first graduate program in endodontics—one of only two in Canada, and the only one in western Canada. He also developed an interactive DVD-ROM, *Endodontics and Traumatology*, a hands-on teaching and learning program now used by universities and dentists around the world.

"We are fortunate to have such a strong dentistry faculty and alumni group at UBC," Haapasalo says. "The dedication and high level of professionalism of BC endodontists is an important cornerstone of our work here at UBC. Students, general practitioners and, most importantly, patients in the community reap the benefits."

Endodontics Primer

Endodontics – One of the nine specialties of dentistry recognized by the American Dental Association (from the Greek *endo*, or inside, and *odons* for tooth).

Biofilm – Colony of numerous, interdependent bacterial species that form a film on the tooth, root and gums causing disease and decay.

Bacterial Morphology – A single bacterial cell has three basic types or shapes: bacillus (little rod), coccus (grain or berry) and spirochete (coiled or helical).