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Unorthodox orthodontics

By: Melinda Sherwood , Business Editor

A Princeton doctor's discovery may give people who wear braces a reason to smile.

People who need braces may one day have local orthodontist Jonathan Nicozisis to thank for their beautiful smiles.

A staff member of the University Medical Center at Princeton who runs a private practice with partner Louis J. Russo, Jr. in Princeton Professional Park, Dr. Nicozisis's research is the basis of technology under development that may significantly reduce the amount of time necessary for people to wear braces.

Dr. Nicozisis is the founding orthodontist and a scientific advisory board member of BAS Medical Inc., a biomedical startup based in San Mateo, Calif., that has acquired the intellectual property rights for relaxin, a naturally occurring hormone that, as the name implies, relaxes the body's connective tissue. Dr. Nicozisis, or "Dr. Nick" as he's often called, first heard about relaxin in a biology class at LeHigh University, where he learned that the hormone's anti-elastin effects during pregnancy help widen the birth canal.

It wasn't until later, during his residency at Temple University, that he realized relaxin's potential application to orthodontics. "I remembered learning about this hormone when I was at LeHigh, and a lightbulb went off," he said.

Two of the major challenges facing orthodontics today, he explained, is the long time braces must be worn, and the tendency for teeth to relapse to their original position after the braces are removed. Most orthodontists attribute relapse to the memory built up within the connective tissues. When braces are put on, these fibers stretch like rubber bands, explained Dr. Nicozisis, but when the teeth get to their final position, these fibers often do not readily remodel.

"When we take the braces off, the teeth tend to move back, but not completely," he said. "Most of that relapse occurs within the first year."

Retainers, if worn regularly, can help minimize the relapse, but "after month three, they (kids) get a little lazy, and then they come in and the lower front teeth are rotated, and it's enough to upset mom or dad," said Dr. Nicozisis.

If the connective tissue is more or less the same throughout the body, Dr. Nicozisis posited, couldn't relaxin help the connective tissue in the gums to release, thereby reducing the likelihood of relapse and the time necessary for people to wear braces?

That's the question he set out to answer for his degree in oral biology. In his master's thesis, Dr. Nicozisis focused on demonstrating relaxin's effects on the connective tissues in the cranio-facial sutures and periodontal ligament of mice. That research demonstrated a strong potential benefit of applying the effects of relaxin to the world of orthodontics.

"It would be wonderful to be able to decrease the time that people are in braces," he said. "If we take a two-year treatment plan, on average, and even if we increase the rate of tooth movement, cutting it down to a year and a half, perhaps a lot more people would be interested in going into orthodontics treatment."

Two years after Dr. Nicozisis's thesis was published, Peter Breining, a California entrepreneur, was doing a Google search on relaxin and the paper came up. The two men began collaborating and BAS Medical was formed.

Local venture capital firm Domain Associates, and Kleiner, Perkins, Caufield & Byers of California, agreed to back the firm if they acquired the intellectual property rights for relaxin, then licensed to two other biotech firms — Connetics Corporation and Genentech Inc. — for the treatment of scleroderma, a debilitating disease that causes the skin to harden. BAS Medical secured worldwide rights for the hormone in July of 2003.

Phase One clinical trials of relaxin to accelerate tooth movement are scheduled to begin later this year at the University of Florida, and if approved by the U.S. Food and Drug Administration, relaxin could be on the market by 2008, said Mr. Breining, CEO of BAS Medical.

That would bring orthodontics out of the 19th century and straight into the 21st century, said Mr. Breining. "Orthodontics is a sort of market that's been stuck in the 1890s," he said. Braces are like "talking to the cells through force and it's a gross way to talk to cells," he said. Relaxin, by contrast, talks to the cells biochemically, "in a way they understand better."

With five million people in braces in the United States and two million patients treated each year in the United States alone,



Staff photo by Mark Czajkowski

Orthodontist Jonathan Nicozisis's master's thesis is the basis for technology being developed by BAS Medical Inc. that would cut the amount of time patients need to wear braces.

the market for relaxin is also significant, added Mr. Breining.

In addition to studying its orthodontic applications, BAS Medical is also investigating relaxin's effects on arterial disease and kidney disease as well as a condition called pre-eclampsia.

One of the most common medical complications of pregnancy, pre-eclampsia is characterized by renal dysfunction and hypertension and often results in the pre-term delivery of a baby. "That's an application we don't disclose as much about," said Mr. Breining, but he added that research in that area is promising.

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