FROM FOREST TO FEMUR

From forest to femur: is rattan the material of the future for bone replacement?

A new Italian tech company is in the final stages of bringing an innovative rattan 'green bone' medical product to the world market.

Rattan brings livelihoods to many forest communities in South and Southeast Asia and West Africa who harvest and transform it to make furniture and household goods. Today, an emerging new branch of medical science – rattan-based bone replacement – is on the verge of creating a brand new high-tech, high-value product. It has the potential to bring better therapy to millions of patients worldwide and new growth opportunities to rattan resource countries and rural communities in the coming decades.

From forest to femur: rattan is approaching clinical trials for European Union approval as a bone implant – a potential market of several billion euro per year.

Millions of people worldwide have bone repair and replacement therapy to combat the effects of conditions such as osteoporosis, bone cancer, and other degenerative diseases, or severe breakages resulting from accidents.

Bone replacement therapy is a well-established science. Current approaches use bone grafts and ceramic and metal alloys, interventions that work well for small bone repair and replacement.

But for larger bone replacements, for three centimeters or more , medical professionals are grappling with the limitations of using the traditional rigid materials. If it could be engineered, the 'miracle' bone replacement material would act like human bone. It needs to be rigid, yet flexible enough to move with the body, and with an internal structure that allows the growth of nerves and blood vessels. Ideally, it would fuse naturally with surrounding bones when implanted in a person's leg or arm and then be transformed in real living bone.

The rattan plant largely fits this description as revealed recently by results of a decade of research by scientists at the **Institute for Science and Technology for Ceramics of the Italian National Research Council (ISTEC-CNR) (http://www.istec.cnr.it/index.php/eng/about-istec)**. The work of ISTEC ceramics researcher, Anna Tamperi and her research colleagues was published widely and **reported** (http://news.bbc.co.uk/2/hi/europe/8446637.stm) six years ago, as they embarked on their first trials of rattan-based bone implants to repair the damaged limbs of sheep. Today, the trial results have been promising enough to progress to human clinical trials, as the final step toward commercialization.

Results confirm that, over time, the rattan bone replacements in sheep are fully integrated in the hosts' bodies, and have fused with the natural bone, explains Lorenzo Pradella, CEO of GreenBone Ortho srl, the Italian high-tech startup he founded last year to complete clinical development and commercialize the rattan technology. "The first animal study showed good indications that the rattan bone will be progressively taken over by natural bone, continue growing and take on natural bone properties. We now expect to confirm this in clinical development," says Lorenzo.

With an abundance of new materials and composites coming out of the science community, why rattan: a traditional forest product that has been around for millennia? Pradella says that the research team tested the assumption that woods – which naturally transfer fluid upward and downward in trees (Xylem and Phloem) – have a similar function as bones, with their 3D skeleton and bundle of nerves, marrow and blood vessels inside. After investigating a range of woods, the research team identified rattan as the material with very similar characteristics to bone. "It has the right dimension and rigidity, but it bends," he says. "Through the microscope, rattan's internal structure looks very similar to that of a human bone."

GreenBone CEO, Lorenzo Pradella

The research compared the contents of various rattan species to the properties of bone, then developed a process transforming rattan into a material that mimics bone's structure and behavior. ISTEC developed a ceramic process that removes cellulose, lignin and other plant materials from the rattan stalk. This leaves behind a carbon skeleton that is treated with calcium and phosphate, producing a porous structure that is chemically and mechanically similar to bone. Tampieri says that unlike metal alloys, polymers or donor bone, their new green bone material is low-cost, readily available, and compatible with existing bone, which helps bone regeneration.

The species of choice for the rattan green bone is Calamus rotang. This variety grows mainly in southern India and Sri Lanka,

along river margins and swamps at low elevation. It is traditionally known as good cane for baskets and furniture, according to rattan specialists at Kew Botanic Gardens, who have compiled extensive global rattan inventories.

Pradella makes a strong business case for large-section bone replacement. "The global orthopedic biomaterials market, valued at $6.5 billion in 2013 is expected to double by 2018 as the demographic in many countries sees a growing older population. Rattan-based bone therapies can catch a healthy percentage of this sector," he says.

As the research comes closer to becoming confirmed, the tipping point for market growth will be to secure a stable, high quality supply of rattan. Current supplies are from a furniture producer in South Asia. Pradella explains that the supply of rattan for GreenBone materials will follow the model for global medical supply procurement, where the raw material is produced by a specialist intermediary company that ensures strict quality, safety and hygiene standards. "There is no history of such a supply chain for rattan for medical use. We are working to understand how this will work and to have a clear idea of resource availability."

In parallel with the clinical trials Pradella and colleagues are fine-tuning the business model, which addresses the key questions: how much rattan will be needed?; is there adequate supply?; and where is it located? It is early to have precise market information. But, as an indication, a scenario of 10,000 implants per year, at six cm per implant, will require an annual supply of 600 metres of raw rattan. Is there enough Calamus rotang readily available?

Rattan harvest: the future supply chain for high-tech medical devices?

Hans Friederich, Director General of the International Network for Bamboo and Rattan, comments that assessing the resource is crucial to the success of any new bamboo and rattan-based business model. "The green bone technology is one of the most novel new approaches we have seen. And every month we hear of entrepreneurs exploring new uses for these plants for innovative businesses and value chains – ranging from bicycles to electricity generation, wine, engineered parts for industry, and many other ideas. Whatever the product or sector, a resource assessment is needed to ensure that the venture has an adequate supply of the primary forest resource."

The initiative, **Global Assessment of Bamboo and Rattan (GABAR)** (http://www.inbar.int/gabar), was recently created by INBAR and its 41 member countries to help produce data and evidence that will support the growth of bamboo and rattan enterprises, the business community and natural resource planners in resource countries. "The questions being considered by Green Bone are a good example of how strategically important a national rattan resource inventory is – to determine the potential of supply that will bring business models to life and support regional economic development plans," says Friederich.

What are the next steps for the world's first rattan-based bone replacement? Human clinical trials start in 2016. GreenBone expects to receive preliminary approval soon to use the technology to help patients in compassionate cases, such as major trauma. The Green Bone team is gearing up to go to market, with approval of European Union medical regulators hoped for 2019.

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