Five or six times a year, Dr. Luca Sangiorgi attends medical conferences across Europe to keep abreast of the latest developments in his field—the use of clinical genetics to improve the diagnosis and treatment of rare bone diseases. In addition to being a practicing physician and a professor of medical genetics at the University of Bologna, Sangiorgi is also the head of the Medical Genetics Department of Bologna’s Rizzoli Orthopaedic Institute and the coordinator of its Rare Disease Center. To Sangiorgi, these conferences provide a prime opportunity to discuss the latest promising new approaches to understanding the complex relationship between genes and rare diseases.

In venues such as this, the most vibrant and illuminating exchanges often take place off to the side, in the specialist breakout sessions, where small groups of colleagues can be more candid, direct and detailed in discussing their work. Where clinicians and researchers can exchange their unique yet complementary perspectives on a shared passion—to better treat, understand and ultimately cure a specific group of diseases. In his experience, Sangiorgi has often seen these discussions give rise to a “wish list” of ideal analytical and diagnostic tools, which—if only they could be made available—would help specialists find a piece of the puzzle that seems to hover just out of reach.

"Smarter healthcare can be collecting data, sharing data and pedigree analytics and [an] altogether better way of life for the patients."

—Marina Mordenti, Researcher, Rizzoli Orthopaedic Institute

**Leadership Spotlight**

At the Rizzoli Orthopaedic Institute in Bologna, Italy, Dr. Luca Sangiorgi leads a team that is using the latest analytical tools to better understand the complex interplay of genetic factors in hereditary bone diseases.

**How Rizzoli got smarter**

One of the big mysteries of hereditary bone diseases is clinical variability—how afflicted people in the same family can show such drastic differences in the severity of symptoms. To Sangiorgi, getting a more granular understanding of the dynamics of clinical variability held the prospect of dramatic breakthroughs in treatments. Rizzoli’s new Pedigree Visualization and Analytics Platform delivers on that promise. Specialists are using the system to optimize their treatment decisions. It’s helping Rizzoli improve the quality of its patients’ lives now, and is expected to reduce the hospitalizations and imaging tests (such as CAT scans and MRIs) by 30% and 60%, respectively, in the near future.

*Let’s Build a Smarter Planet*
Getting to the roots of hereditary disease

It was that kind of discussion that led Sangiorgi and his team of researchers at Rizzoli to conceive of an analytical tool that had the potential to fill in critical gaps in their understanding of the workings of certain hereditary rare bone diseases. One central question lay at the heart of the mystery: In families where such diseases are carried in the genes, how can it be that family members affected by a disease express its symptoms with major differences in severity, with some family members barely affected and others barely able to function?

On a strictly research level, the correlation between a patient’s genetic predisposition to a hereditary disease (genotype) and how that disease actually develops and manifests (phenotype) provides a valuable window into the complex genetic interactions that lead to disease. But that isn’t the main interest that drives the efforts of Sangiorgi and his team. Since most hereditary bone diseases are neither fatal nor curable, the challenge for physicians is to manage the disease to enable the best possible quality of life for the patient over their entire lifespan. That means providing the right level of ongoing treatment for each patient based on the specifics of their prognosis. Having an ability to find that balance is seen as essential in the quest to improve the quality of patients’ lives.

The quest for optimized treatment

In his capacity as a physician, Sangiorgi saw firsthand how the impact of bone diseases on patients can extend beyond the pain and disfigurement caused by clinical symptoms. Much of this impact, he believes, can be attributed to a tendency for physicians to, in effect, “over treat” patients because they lack the clinical insights they need to match the intensity of the treatment protocols with the patient’s actual underlying needs. “Even though severe manifestations are seen in just one-third of bone disease patients, physicians have had little recourse but to apply the most intense—and disruptive—treatment protocols to nearly every patient,” says Sangiorgi. “As a result, the majority of patients incur an extra cost—in their quality of life—beyond the impact of the disease itself.”

One of these costs is the inconvenience of travel. Because most local hospitals lack the knowledge and resources needed to address rare bone diseases, patients and their families often have to travel hundreds of miles by plane or train to receive follow-up treatments at specialized institutions like Rizzoli. The more frequently these distant follow-ups are scheduled, the greater the inconvenience and cost incurred. The perceived obligation to follow a conservative treatment protocol for all patients also tends to increase the frequency of imaging procedures, such as CAT scans and MRIs, and make physicians more likely to recommend major surgery. In addition to adversely affecting the patient’s quality of life through possibly needless tests and procedures, this upward bias also puts upward pressure on healthcare costs.

The benefits of Rizzoli’s pedigree analytics capability

• Expected 30% reduction in surgery-related hospitalizations due to more evidence-based surgery protocols
• Expected 60% reduction in imaging requests
• Reduced need for patient travel through optimization of follow-up treatment scheduling
• Enhancement in patient quality of life due to all of the above factors
• More effective treatments for hereditary diseases through more targeted protocols
• More accurate determination of hereditary disease risks
Rizzoli’s path took a turn when Sangiorgi and a small group of his clinical and research colleagues went on what could be described as a week long “learning mission” in Haifa, Israel, a hotbed of healthcare technology innovation. Having heard about “interesting things” that IBM’s Haifa Research Lab was doing in medical analytics, Sangiorgi set in motion a series of meetings that produced—in a matter of hours—the basic framework for achieving a goal he had been aiming at for years. That framework ultimately evolved into a solution known as the Pedigree Visualization and Analytics Platform, a powerful analytical tool that integrates genomic and phenotypic profiling capabilities with family medical history data—the “three legs of the stool” in probing the complex interactions underlying hereditary diseases.

The idea for the platform gestated for about a year, during which Sangiorgi and key colleagues worked to fine-tune it before bringing it before Rizzoli’s key decision makers for approval. It was during this span that he returned to Haifa, this time in the company of Rizzoli’s Chief General Officer, Giovanni Baldi, MD, who—intrigued by what he had heard from Sangiorgi—had come to get his own first hand demonstration of what the proposed system could do. After hearing a three-hour presentation of its planned capabilities, Baldi came away favorably impressed. Sangiorgi, as the project’s primary sponsor, gained an important ally.

Ultimately, Sangiorgi needed to make his case to three key figures within Rizzoli. In addition to Baldi, there was Scientific Director Francesco Antonio Manzoli, MD, PhD, whose primary focus was the impact on Rizzoli’s research capabilities, and Administrative Director Dr. Antonio Sasdelli, to whom the project’s financial case was of principal importance. In order to mirror Rizzoli’s mission focus as an organization, Sangiorgi framed the business case in terms of the solution’s research and clinical benefits, all under the overarching goal of improving his patients’ quality of life. In the end, the fact that Rizzoli’s top leader had become a believer in the project contributed in a meaningful way to its ultimate approval.

In order to mirror Rizzoli’s mission focus as an organization, Sangiorgi framed the business case in terms of the solution’s research and clinical benefits, all under the overarching goal of improving his patients’ quality of life.
About a boy: the evidence of success

Of the thousands of patients Rizzoli treats each year, one case stands out as the epitome of what Sangiorgi and his team had sought to achieve with the pedigree analytics solution. About 100 miles from the institute, physicians at a local clinic were evaluating a six-year-old boy afflicted with a hereditary bone disease that caused pronounced deformity. Unsure of the best course of action—but inclined to perform major corrective surgery—the clinic’s physicians decided to send the boy’s information to specialists at Rizzoli. Because Rizzoli sees about 300 patients with such symptoms every year—compared to perhaps 10 for the average local clinic—it was able to compare the boy’s case with a cohort of 600 patients with a similar clinical presentation.

By analyzing genomic data, detailed imaging tests and case histories, Rizzoli specialists were, in effect, able to look into the boy’s future by extrapolating the likely course of the disease’s progression. Through the insights they gained, the specialists concluded that the boy’s future would be best served with minor surgery, which would spare him and his family the burden of weeks of hospitalization and subsequent follow-up care. Just weeks later, the boy was back in his hometown, where a local surgeon—who had reviewed Rizzoli’s analysis—successfully performed the minor surgical procedure that got the boy home in a matter of days.

Unsure of the best course of action—but inclined to perform major corrective surgery—the clinic’s physicians decided to send the boy’s information to specialists at Rizzoli.
A foundation of flexible integration

This example illustrates how, in the case of chronic illnesses, clinical decisions based on diverse data and powerful analytics can have a major impact on quality of life. What makes it possible is the solution’s unique ability to gather diverse and detailed information on specific cohorts of patients, and to use this base of information as a means to drill down deeper into the genetic dynamics of hereditary diseases. Because it uses open interfaces such as HL7 and DICOM, the Rizzoli solution is capable of integrating data not only in multiple hospital systems and formats, but also from other hospitals, clinics and data sources.

In the near term, Rizzoli also expects its ability to optimize treatment protocols for hereditary bone diseases to lead to much more efficient and cost-effective care. For instance, by leveraging the Pedigree Visualization and Analytics Platform to determine the most appropriate surgery—and thereby avoid unnecessarily invasive procedures—Rizzoli expects to reduce associated hospitalizations by 20 percent in the first year and 30 percent thereafter. What’s more, because the solution will enable physicians to set evidence-based protocols for imaging requests (as opposed to applying “worst-case” protocols as the default), Rizzoli expects to reduce the overall number of such tests by more than 60 percent.

In the longer term, Rizzoli expects the analysis of clinical variability within family trees to yield far deeper insights into—and potentially cures for—rare hereditary bone diseases. To Sangiorgi, the solution exemplifies the new tools researchers are applying to solve an old puzzle. “Understanding the complex roots of hereditary diseases requires a whole new way of looking at pedigree analytics,” says Sangiorgi. “With the Pedigree Visualization and Analytics Platform, we’re beginning to learn the most effective ways to treat hereditary diseases and, most importantly, we’re making a meaningful impact on the quality of our patients’ lives.”

Rizzoli’s pedigree analytics solution is…

**Software**
- IBM® Enterprise Content Manager,
- IBM WebSphere® Application Server,
- IBM InfoSphere® Warehouse,
- IBM Tivoli® Directory Server,
- IBM Tivoli Storage Manager

**Servers**
- IBM System x®

**Services**
- IBM Haifa Research Lab, IBM First-of-a-Kind Program

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