Every discipline has its Masters.

GIORGIO BRUNELLI, an eclectic surgeon, was a Master in the history of medicine. He was a great orthopedic surgeon, a world pioneer in microsurgery, and a passionate researcher of the central nervous system and its plasticity.

Intelligence, and not only in its most extreme form of genius, is often expressed in the most diverse and unimaginable ways.

This was the case with Giorgio Brunelli, a world-renowned Orthopedic and Microsurgeon. He was a pioneer in these fields, as well as in the fields of Implantology and Basic and Applied Research in the treatment of spinal cord lesions.

Brunelli's work has been praised internationally, and he has been recognized by Nobel Prize laureates, such as Rita Levi Montalcini, who sponsored his candidacy for the Nobel Prize for Medicine, for his contributions to Basic and Applied Research and our understanding of the CNS, where he rejected the common belief that the brain should be investigated by just a restricted group of specialists, such as Neurologists, Anatomists, Neurosurgeons and Physiologists.

"Brunelli showed," the Nobel laureate said, "how little we used to know about neuronal plasticity and the advantages to be achieved if we could understand it better."

His decision to study medicine was inspired by his service in the Army during the war when he worked in a small field hospital. At least this is what most people know about it. However, he confessed to a few intimate friends that, upon his return from the war, he was totally unaware whether his father—the Chief Veterinary Doctor at the slaughterhouse in Brescia—had enrolled him in the School of Engineering or the School of Medicine. Planning ahead, he studied to take two tests that would have been useful in either case: Chemistry and Physics. When he went to the University of Parma, he discovered that he had been enrolled in the School of Medicine. Despite those uncertain and turbulent times, amazingly, Brunelli graduated on time, in 1949, after 6 years of study. Unfortunately, he did not graduate with top grades, as he described in his autobiography:

My Doctoral work was a histologic study on “Synovial Joints” drafted with Prof. Marcer, a great Orthopedist, one of the few to perform pollicization of the index finger on veteran “amputees”, a procedure that back then seemed a miracle since it restored grip to the thumb. My doctoral dissertation had been very carefully prepared, and I was sure that I would get the top 110 “cum laude” mark. Unfortunately, Prof. Marcer—who in 1945 replaced Prof. Bocchi because the latter was a fascist—had to leave his Chair on the eve of my dissertation, since Prof. Bocchi had been reinstated. So, Bye-Bye to my “cum laude” and I had to make due with “110 /110”.

His experiences during the war inspired the young doctor to pursue Orthopedics.

Academic Career
Brunelli enjoyed a very rapid and successful surgical and academic career: Chief of Surgery at age 35, University Chair in 1971. Yet, the most striking of Brunelli’s achievements is his pioneering work, such as the first hip joint prosthesis replacement surgical technique in Italy in 1963, and Microsurgery, introduced in Italy in 1965. He was officially acknowledged as one of the top 5 leading pioneers worldwide. He performed the first brachial plexus surgery in 1972, and the first total limb re-implant in Europe in 1973. He earned an Honoris Causa Degree from the University of Wroclaw and in the 1980’s, he focused on experimental research to try to cure spinal cord and paraplegic lesions.
Of those years, he wrote:

At the end of the 1970’s, many patients suffered from arthrosis of the hip, and there weren’t enough orthopedic surgeons to treat them. In Brescia, we had reached a level of excellence in this setting, and we had patients coming in from all over, especially from Southern Italy. In those years, our surgical ward wasn’t big enough to host all of these patients, who came with the hope of being added to the surgical list as soon as possible.

There were many young paraplegic patients who came to my hospital ward in the hope of finding a solution to the problems with their legs, like we did for paralysis of the brachial plexus; yet, all the experiments carried out until then on animal models unfortunately showed that the bone marrow would not receive exons from the brain. I persisted, fully believing that I had to take up the challenge, and continued my research on bone marrow repair. I set up the Spinal Cord Lesions Foundation and began laborious and difficult research on the anatomy and physiology of the bone marrow and its chances to be cured after a lesion.

Teaching Young People

Teaching was always a very important part of Brunelli’s professional life. He was the ideal conduit for the thoughts and teachings of his Italian and foreign instructors: Prof. Poli from Milano, Prof. Merle D’Aubigné from Parigi, Prof. Tunnel from the U.S., as well as Prof. Böhler from Wien and Prof. Möberg from Göteborg.

For him, teaching was always a great source of excitement and dedication: “I have always believed I had to teach to the best of my ability and, except for a quarrel in 1968, I had always entertained a friendly relationship with my students”. This is a reference to a peculiar episode that occurred upon the foundation of the University of Chieti. Back then, he was working as an Orthopedic Surgeon at the Ospedale Policlinico SS Annunziata in Chieti, and had been called to teach anatomy and human physiology. During an exam, he asked a student to describe the femur, and the student answered “a long bone beginning at the level of the hip and ending to the foot”. Of course, the student didn’t pass. Outside the classroom, Brunelli found a group of students ready to attack him. Fortunately, he was rescued by some other students who had passed the exam.

His scientific “forma mentis” allowed Brunelli to always respect scientific thinking, research and critical assessment of the patient’s data as well as treatment, medical and surgical options. This was particularly true for the field of hand surgery, which encompassed several innovations, including microsurgery, noninvasive surgery, protheses of the various joints, metal and plastic materials for surgical use, robotics and a closer relationship between orthopedics and recent scientific discoveries.

Medical training and work require years of sacrifice and, as Brunelli used to say, “young doctors must be prepared to make many sacrifices, must know that money does not come easily, and must be aware of how much they must give up if they want to be thorough and well-trained doctors.”

Brunelli also used to advise young doctors to spend some time abroad, which he regarded as being key: “Not because we lack structures and skills; but rather because the experience we can gain is so varied that we can add to our professional skills anywhere in the world.” For him, working abroad could be a long post-doctoral stay—which might hinder one’s return home — or short breaks in different hospitals to learn super-specialized techniques, following a post-doctoral period in an Italian hospital. Younger generations of doctors are always associated with an infusion of new techniques, to the benefit of all: “the new generations, while attending college, can bring in new IT knowledge which simply did not exist when we were young, and can therefore have easier and faster access—thanks to new technologies—to scientific discoveries, which when I was young was not even thinkable, and this was one of the reasons why publishing a scientific work used to be both a hard and prolonged exercise”. Brunelli knew all too well how many hours could be spent in university libraries looking for references that can now be accessed by just one “click”. He wrote that “(a)ll this will allow doctors to make giant strides ahead in their scientific learning and careers.”

Research insights of a genius

Brunelli’s full-fledged research efforts on bone marrow began in the 1980’s. His first insight was that, once damaged, bone marrow cannot be repaired. Always with the goal to restore movement of his patients’ lower limbs following traumatic events, he was the only Italian to enroll in the European project SUAW (Stand Up And Walk). It was carried by all the media; a young man who could walk due to the presence of microelectrodes implanted—by Brunelli himself—into his muscles and driven by an external stimulator. Unfortunately, the project was discontinued to a lack of funds. Brunelli returned to surgery to circumvent axons that could not make their way through the bone marrow and though to move the ulnar nerve from an arm to the muscles of the pelvis and thighs, which are important for stabilizing the pelvis frontal plane and gait. This technique, which was first tested on animals, was ultimately tested on a patient, fully informed and with the approval of the Ethics Committee. This was the only solution that medicine could offer back then. The patient, Angelo Colombo, was and still is proud—as he himself says—to have made his body available to science: “Surgery was fully successful. At the beginning, when I wanted to walk and extend my knees, I had to think to move the fingers of my hand which were fed by the ulnar nerve. After a period of intense
rehabilitation, based on the plasticity of the CNS, I could walk more spontaneously and automatically, although my movement was still rudimentary.”

Research was progressing with giant strides and, after years of testing with different surgical protocols both in Italy and abroad, Brunelli decided to connect—through a nerve graft—the extensions of the brain cells to the nerves of muscles of the pelvis and legs, bypassing the spinal cord below the lesion. This was the technique used with a young lady who—following a road accident—had a total lesion of the spinal cord at the level of the 8th thoracic vertebra. After surgery and a period of intense rehabilitation, she started to take her first few steps, although not entirely smoothly, first with the help of a walker and later with a tetrapod. This was because the extensions of the brain cells, when they reached the muscles, formed new motor-plaques that could respond to the neurotransmitter glutamate in the CNS, but not to acetylcholine, which is found in the periphery. This response to glutamate was totally unexpected and prompted Brunelli to continue his research, which—thanks to the valuable advice of Prof. Montalcini—became an actual basic and multi-disciplinary research effort, involving scientists from the University of Brescia: “Through these studies, we proved that muscle could change its normal acetylcholinic receptors to those that could respond to glutamate, which is a neurotransmitter for neurons of the brain.” On June 14, 2005, the official journal of the U.S. Academy of Sciences (P.N.A.S. 2005, 102, 24, 8752-8757) published the results of this research.

In 2006, another prestigious journal from the U.S., Current Opinion in Neurobiology, published an article entitled “A lost paradigm,” which clearly referred to this previous finding, in that, while one paradigm was lost, a new truth was revealed. The reason for all of this dedication, of course, is that a beautiful young lady now had an opportunity to be self-sufficient and lead a nearly normal life.

Research is like a never-ending story, in that for each research protocol that comes to an end, another opens up. Based on an analysis of the experimental results, another mystery became evident: the connection with the grafts was achieved by connecting the graft with the corticospinal tract of the spinal cord completely at random.

In the corticospinal tract, several thousands of fibers descend from different areas of the cerebral cortex and have different functions. Therefore, one might expect that the resulting movements could be global, and all muscles connected to the corticospinal tract of the spinal cord would be contracted at the same time, without a functional outcome. On the contrary, and against all odds, at the beginning of re-innervation and after a few months following surgery, the animal subjects as well as the patient who consented to undergo surgery, were able to achieve discernible voluntary, useful and unconstrained movements. The explanation for this finding is that there is a presently unknown feedback mechanism that allows the instructions from the frontal lobes to recognize the motoneurons in the brain cortex that have been peripherally connected to the muscles that must be contracted (without tedious co-contractions), and excites them selectively.

Research proves that the resulting movements do not depend upon the activation of a cortical area, but rather on the excitation of millions of single neurons scattered throughout different areas of the brain cortex. fMRI has demonstrated that the instructions for single movements do not arise from a small cortical area, but rather that the whole motor area is affected, which supports the plasticity of multiple neurons scattered throughout the brain cortex. Based on these results, Brunelli assumed that brain plasticity was not due solely to the changes in brain areas with different functions—this has been known for more than a century because of the results of muscle-tendon transfer due to partial paralysis of the limb—but also to the change in function of millions of motor neurons scattered throughout the brain cortex, which could be selectively activated for movements that, before surgery, could not be performed. If we take into account our still incomplete knowledge of the anatomy and physiology of the spinal cord, it is evident that these results are only the beginning of the surgical treatment of paraplegia and possibly other bone marrow lesions.

“This is a long and uneven beginning which can only be surpassed through many other future research efforts…”

Giorgio Brunelli performed over 25,000 surgical procedures, 3,500 of which involved microsurgical techniques. He authored 466 papers in peer-reviewed journals, 30 book chapters and 10 scientific texts.

Besides his scientific and surgical work, Giorgio Brunelli was a successful athlete in various disciplines, including fencing and swimming. He was a regional university champion at cross-country skiing in 1948. He loved vintage cars and, as a gentleman driver, participated in various races and several Mille Miglia.

Brunelli loved Nature in all its expressions, which he captured with both his Nikon and his paintings. To say that he was an amateur painter doesn’t quite capture his talent. Several exhibitions of his paintings and photos were organized over the years. He also published several historical novels as well as, due to his intellectual passion for the neurosciences, scientific essays, such as “From Neurons to the Self” and “Conscious Ego”.

Profits coming from all his different projects were channeled to his Foundation and research projects which will continue, following the path he blazed.