BRACCO FELLOWSHIPS EDUCATION IN RESEARCH

Name of the Institution: Department of Clinical and Experimental Medicine, University of School of Medicine, Foggia (Italy). / Radiology Unit "Dimiccoli" Teaching Hospital, Barletta, Italy.

City and Country of the Institution: Foggia, Italy.

RESEARCH GROUP

Brief description of the research group and of its mission:

Chief:

Prof. Giuseppe Guglielmi (Full Professor; scientific and disciplinary sector - MED/36 - Diagnostic Imaging and Radiotherapy).

Prof. Guglielmi's research focuses on Molecular Imaging, Digital Radiology Diagnostics, Computed Tomography, Magnetic Resonance, Bone Densitometry, Radiomics, and Radiogenomics.

The study of bone metabolic diseases, rare diseases, geriatric radiology was the focus of his activity in the field of Musculoskeletal Radiology, with particular attention on integrated high-resolution imaging (DXA, US, CT and MRI) for the evaluation of the trabecular bone network and the analysis of the body composition. Forensic Radiology represents another subject of interest, in collaboration with forensic doctors on the Virtopsy project (virtual autopsy) and on the following Virtangio project (virtual angiography) which made it possible for the University of Foggia to be included as the only Italian branch of the Post-Mortem Angiography project in Europe. Finally, since 2003 the position of Radiology and Radiographics RSNA Editorial Fellow represents a further field of interest in the editorial activity (medical writing). This position enables one to engage in significant editorial activity as Editor-in-Chief, Deputy Editor, and Member of the Advisory Board of numerous national and international Radiology journals. Numerous scientific publications, presentations at scientific conferences with both national and worldwide relevance, book chapters and educational initiatives have resulted from these challenges.

TITLE OF PROPOSED RESEARCH PROJECT:

Radiofrequency Echographic Multi-Spectrometry (REMS) technology for bone health assessment (quantity and quality information) and Fracture Risk prediction in patient with multiple myeloma

Bone disease is a important characteristic of multiple myeloma (MM), the most common type of hematological disease characterized by the autonomous monoclonal proliferation of plasma cells in the bone marrow4.

MM manifestations are usually identified through lytic lesions associated with severe pain, pathological fracture, spinal cord compression, vertebral collapse, and hypercalcemia3. At least 85% of MM patients show some degree of osteopenia[9] at diagnosis, approximately 60% of MM patients develop a fracture during their disease course [1,10] and the severity of bone destruction typically correlates with tumor burden and prognosis.

A compromised bone micro-architecture (from the intensified osteoclast activity and bone resorption) decreases quality of life in patients, increasing both morbidity and mortality.

Thus, missing out on prevention and diagnosis of bone disease can be very detrimental to the patient's health as well as to society. Actually, the detection of lytic bone lesions with imaging (especially computerized tomography (CT), Magnetic Resonance Imaging (MRI) etc.) and osteoporosis diagnosis measured BMD amount (by DXA and REMS) are becoming crucial and essential from the clinical viewpoint for the management of patients with MM.

For assessment of osteoporosis Dual X-ray absorptiometry (DXA) has been used as gold standard. Unfortunately, there are several limitations related to the DXA examination, such as the accessibility, restrictions in personnel allowable to perform scans, large size and the need for a dedicated room, limited accuracy– dependent operator, impossibility of monitoring the short-term effectiveness of the treatments and late diagnosis. Moreover, risk of fracture is underestimated for the presence of unrecognized artifacts.

Additionally, it's necessary to consider that MM patients are vulnerable due to the therapies they got and exposed to different risks including cumulative radiation exposure, radiation-induced cancer risks by ionizing-radiation.

In order to improve their life expectancy reducing exposure to additional ionizing radiation and allowing bone health status short-term monitoring, alternative diagnostic promising tools in the treatment of MM-derived bone disease must be evaluated.

Nowadays, the limitations previously mentioned can be overcome[2,5,6] through an non-ionizing technology called Radiofrequency Echographic Multi Spectrometry (REMS). These considerations make it evident that early and prevention diagnosis is necessary to mitigate the impact of osteolytic bone disease in the context of MM progression. The opportunities offered by ultrasound technology REMS in patients affected by multiple myeloma are several. Indeed, REMS technology enables to assess the bone health status by a quick and non-invasive echographic scan to be performed for the diagnosis of osteoporosis on axial anatomical reference sites (lumbar spine and proximal femur). Immediately after the scan, an automatic processing of the acquired signals allows to identify and analyze the target bone structure and the internal region of interest.

The analysis of native unfiltered ultrasound signals allows to retain the maximum information about the characteristics of the investigated tissues, which are normally filtered out during the conventional process of B-mode image reconstruction. The bone health status is assessed through the comparison of the spectra profile of the patients with previously derived reference spectral models for the considered pathological and normal conditions.
REMS does not only estimate a typical bone-quantity measurement such as BMD, T- and Z-Score but it can provide information about bone quality through Fragility Score,[7,8] an innovative REMS-

based parameter more closely related to the skeletal frailty and the status of bone microarchitecture.

The precision and diagnostic accuracy of REMS have been already validated in numerous scientific works. Therefore, thanks to scientific evidence demonstrating the effectiveness of the REMS technology on more than 15.000 subjects in several clinical studies, REMS will allow the preventive diagnosis of osteoporosis and fractures risk, through short-term monitoring on MM patients, not subjecting them to additional radiation exposure. For these reasons, this is a significant advance for preventing skeletal-related events (SREs) such as pathologic fracture, irradiation or surgery on bone, or spinal cord compression and for reducing the progression of MM bone disease.

OBJECTIVES:

• Quantitative assessment of bone mineral density (BMD) deficiency in multiple myeloma patients, (**diagnosis of osteoporosis** by using REMS Technology);

• Qualitative assessment of microstructure changes of trabeculae through **Fragility Score** based on REMS technology in MM patients;

• Evaluation of REMS's ability for detecting MM patients at high **risk of fracture**;

• **Preventing** bone loss at an earlier time point, improving the overall survival and quality of life of MM patients;

• Short-term **monitoring by REMS**, through diagnostic follow-up, of any changes in bone structure as a result of various therapeutic treatments.

APPLICANT'S DUTIES:

• Patients recruiting according to the enrolment criteria (i.e. multiple myeloma patients, age between 21 to 90 year, both women and men, signed informed consent);

• Diagnostic investigation with REMS on lumbar spine and/or proximal femur;

• Data processing, data analyses and management in collaboration with CNR-IFC (Lecce, Italy);

• Attending regular research meetings and journal clubs. Getting familiar with the current literature;

• Preparing national and international scientific publications.

APPLICANT'S BENEFITS:

• The fellowship will lead to a wider understanding of clinical research and research methodology and will lead to learn to acquire and manage data, to review images or

procedures, to search for biases, to develop skills in tools and post-processing and to collaborate with statisticians/clinicians/clinical scientists;

• Collaboration in writing articles and participation on scientific outcomes of preventing bone loss and fracture risk in patients undergoing MM treatments through monitoring and short-term monitoring with REMS technology;

• Drafting oral/written presentations, participation on international congresses and publications with chance of discussing scientific presentations;

• In addition, a higher degree of confidence in exploiting the benefits of REMS technology (radiation free) to limit radiation exposure for MM patients.

Project Leader: Prof. Giuseppe Guglielmi

Members: Testini V., Guerra F., Mannatrizio D., D'Arma G., Fascia G., Gifuni R., Masciavé M., Masino F., Montatore M., Muscatella G., Sciacqua A.

LITERATURE:

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