DIABETIC RETINOPATHY: FROM UNDERSTANDING TO PREDICTION; FRANCESCO BANDELLO, ROSANGELA LATTANZIO, MARIA VITTORIA CICINELLI

State-of-art and future development/perspectives of the research area at international level (max 2000 characters):

The VISION FIRST: Clinical Research Group at the Department of Ophthalmology, Scientific Institute San Raffaele -University Vita-Salute is dedicated to conducting clinical research activities in Ophthalmology with the highest quality standards and following the European and International directives for clinical studies. The Ophthalmology Unit of San Raffaele Hospital is a high-volume third-level referral center for retinal diseases. On average, hundreds of patients are managed, and more than 4,000 ocular diagnostic imaging procedures are performed each year. Our department has been using an ophthalmology electronic health records (EHRs) system with specific modules for retinal diseases and since 2013 (nLIFE, NIDEK, Albignasego (Padova) – Italy). The demographic and clinical data of all the Medical Retina patients presenting at our department have been stored in the EHR system since then. At last review (2021), it holds around 175,746 visits from 11,609 patients.

All the medical retina patients undergo state-of-art multimodal imaging of the posterior segment that allows the study of the retina structure and its circulation with a quasi-histologic resolution. Furthermore, the department is involved in phase II and phase III randomized clinical trials testing innovative therapeutic strategies (drugs, treatment schedules, and treatment delivery strategies) for preventing or treating diabetic retinopathy and its sight-threatening complications, namely diabetic macular edema and proliferative disease.

Actual lines of research (as is) of the Diabetes Research Institute (max 2000 characters):

The research of the VISION FIRST: Clinical Research Group mainly focuses on diagnostic features, prognostic biomarkers, and treatment outcomes of diabetic retinopathy and diabetic macular edema.

Clinical research involves different groups of patients, such as young subjects with type 1 diabetes undergoing annual screening for diabetic retinopathy, subjects with type 1 diabetes with rapidly progressing diabetic retinopathy, or older patients with a long history of either type 1 or type 2 diabetes and no signs of retinal disease. A large subgroup of patients included in our research includes patients with diabetic macular edema undergoing intravitreal injections of anti-VEGF or corticosteroids, with several randomized clinical trials.

Finally, the VISION FIRST: Clinical Research Group is involved in a multicentric clinical trial aiming at understanding early neurodegeneration in diabetic retinopathy and cooperates with the Cardiometabolism and Clinical Trial Unit in evaluating the clinical effects of novel treatments options for diabetes.

Strengths of the research area (as is) of the Diabetes Research Institute (max 2000 characters):

The joint effort of researchers from multiple disciplines is the main strength of the DRI.

Strengths of the VISION FIRST: Clinical Research Group are a large number of patients, the advanced non-invasive ocular imaging devices, and the electronic system for medical data storage. These tools represent precious instruments to build an extensive database of diabetic patients.

Weaknesses of the research area (as is) of the Diabetes Research Institute (max 2000 characters):

Potential weaknesses at the VISION FIRST: Clinical Research Group include a lack of dedicated space or dedicated personnel for research (research subjects often mix with regular patients during the working days). This may limit the allotted time for each patient. Another potential limitation is the relative difficulty in finding naïve diabetic retinopathy patients to include in the research. As the San Raffaele Institute is a third-level institution, we often see patients already treated elsewhere. Finally, fragmentation in delivering diabetes care services is another possible drawback of our group.

Short-medium term OSR/UniSR goals (0-18 months): milestones and deliverables (max 1000 characters):

Short-term projects are aimed to explore the morphologic features of diabetic patients with multiple imaging modalities (e.g., ultra-widefield optical coherence tomography scans, widefield optical coherence tomography angiography) and their functional correlations (with electrophysiology tests or microperimetry). In the last years, publications from the VISION FIRST: Clinical Research Group have allowed better characterization of multiple features of diabetic retinopathy, including microaneurysms, diabetic choroidopathy, and macular ischemia.

Medium term OSR/UniSR goals (18-36 months): milestones and deliverables (max 1000 characters):

Medium-term projects are expected to provide a large amount of data about diabetic retinopathy and diabetic macular edema treatment response to different therapeutic options, including different drugs (intravitreal anti-VEGF agents, dexamethasone implant, or fluocinolone acetonide implants), treatment schedules, and treatment delivery strategies. Timepoints are 1 year, 2 years, and 3 years.

Long term OSR/UniSR goals (36-60 months): milestones and deliverables (max 1000 characters):

Long-term studies target patients with diabetes with no or early diabetic retinopathy, who currently undergo annual screening with dilated fundus exam by an ophthalmologist.

We would like to screen these subjects with additional multimodal imaging modalities, including:

1) OCT angiography, which would help in:
- identifying the early changes in the retinal vasculature occurring in diabetic subjects.
- identifying the perfusion parameters potentially associated with an increased risk of developing diabetic retinopathy or macular edema on long-term follow-up
2) structural OCT, which would help in clarifying the relationship between vascular involvement and neurodegeneration, expressed as thinning of the neuroretinal layers.
3) widefield fundus camera, which is useful for:
- clinical records
- diabetic retinopathy staging, which is nowadays done on fundus photography
- the development and the training of artificial intelligence tools for future screening of early ocular complications of diabetes.

Investments of the Diabetes Research Institute (e.g. personnel, space, technology) to achieve the short-medium-long term goals (max 2000 characters):

Required total investments include:
• two physicians, expert in retinal diseases to coordinate the research and visit patients
• two technicians, expert in ophthalmic photography to acquire multimodal imaging from each patient
• non-invasive imaging systems to evaluate the structural retinal changes in diabetic retinopathy
• ultra-widefield fundus camera to document retinal lesions
• one researcher to collect, analyze and divulge the research data.