PhD Thesis title: 'CMOS active pixel sensors in bio-medical imaging'

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ABSTRACT:
Bio-medical imaging is a large umbrella term which covers a number of different imaging modalities used in healthcare today, spanning pre-clinical imaging, to diagnostic imaging, and imaging to assist and plan patient treatment. This field of research is pivotal to driving advances in healthcare. This is underpinned by advances in new detector technologies, which have the potential to reduce image acquisition time and dose, improving image quality, and offer more accurate tools for diagnosis and treatment.

Large area Complementary Metal-Oxide Semiconductor (CMOS) Active Pixel Sensors (APSs) have the potential to deliver these advances in such demanding and continuously evolving field; large imaging area, together with low noise, low cost, fast readout, high dynamic range, and potential for in-pixel intelligence. All these advances have made this technology an ideal candidate to displace currently used imaging technologies in this field.

This thesis represents the first investigation into the capabilities of large area CMOS APSs to be used across a number of different imaging modalities in bio-medical science, spanning protein imaging to proton Computed Tomography (CT), using both ionizing and non-ionizing radiation sources. A novel characterization of the detector performance has been carried out and set into context of commonly used detectors for bio-medical imaging. Considering the performance parameters assessed for this detector, in comparison with digital detectors commonly used in the clinical practice, this demonstrates how such large area sensor technology may be successfully employed in bio-medical imaging.

The novel large area CMOS APS, studied in this work, is proposed as a multi-modality imaging platform for use in pre-clinical science. For the first time, direct "contact print" imaging of radioactive and optical labeled biological samples on a large imaging area has been demonstrated, showing its potential application to a broad range of ionizing and non-ionizing imaging probes. The protein detection capability of this detector has been compared with both film emulsion and commercially available digital systems, demonstrating a higher resolution in protein detection than either film emulsion or a commonly used commercial western blotting detection system based on Charge-Coupled Devices (CCDs). Also, when detection capabilities of this imaging system are compared with the state-of-the art devices for tissue autoradiography, this detector system exhibits a

sensitivity comparable to that reported for its competitors, whilst offering the largest imaging area. Both these proof of concepts pave the way for large area CMOS APSs to be used as a multi- modality imaging platform in life science.

The radiation hardness of a novel large area CMOS APS, designed for medical applications and hardened-by-design, is presented. The radiation damage, produced in this sensor by X-ray and proton irradiation, has been studied as function of total ionizing dose and displacement damage dose. The damage contributions from ionizing and non-ionizing energy deposition have been separated for the proton field and proved independent from proton energy providing a further verification of the Non Ionizing Energy Loss (NIEL) scaling hypothesis. The lifetime of this detector for routine use in clinical practice has been evaluated as high as 4 years when used in a typical Mega-Voltage radiotherapy environment, demonstrating how such large area sensor technology may be successfully employed in X-ray and proton based imaging applications.

The feasibility of using CMOS APSs, as energy-range detectors in proton CT, has been demonstrated. Capability of single proton counting, together with potential of energy deposition measurements, have been demonstrated for CMOS APSs. Furthermore, experimental work, based on a simple stack of two CMOS sensors, as well as simulation work, has been carried out to prove the capability of such a detection system for proton tracking. Novel algorithms have been developed to perform proton tracking in a CMOS energy-range telescope designed to perform proton CT, paving the way for a new generation of imaging devices to be used in this application.

Key words: CMOS APS, Wafer Scale Sensors, Bio-Medical Imaging, Autoradiography, Western Blotting, Chemiluminescence, Radiology, Mammography, Radiation Hardness, Monte Carlo Simulations, Charge Transport, Proton Therapy, Proton CT

References to author publications that relate specifically to the dissertation:

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