Institution: University of Lincoln		
Unit of Assessment: 9 - Physics		
Title of case study: Large Area CMOS Imagers for Medical and Scientific Applications		
Period when the underpinning research was undertaken: 2011 – 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
ALLINSON Nigel	Distinguished Professor	1 Jan 11 to date
ESPOSITO Michela	Senior Lecturer	1 Jul 18 to date
WALTHAM Chris	Senior Design Engineer	2 Apr 12 to date
Period when the claimed impact occurred: 2012 to date		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

CMOS imagers are at the heart of every smartphone camera and nearly all photographic cameras. Research, led by the University of Lincoln, extended the application of these imagers primarily to medical and scientific imaging – but up to 400 times larger than an iPhone imager and able to withstand harsh exposure to ionising radiation. Working with *ISDI Ltd*, together we produced the first wafer-scale (nearly 13 cm square) radiation-hard CMOS imager. The company built upon these foundations to become the world's third largest CMOS design house and supplier of medical-grade CMOS imagers, with a current annual turnover in excess of £12m.

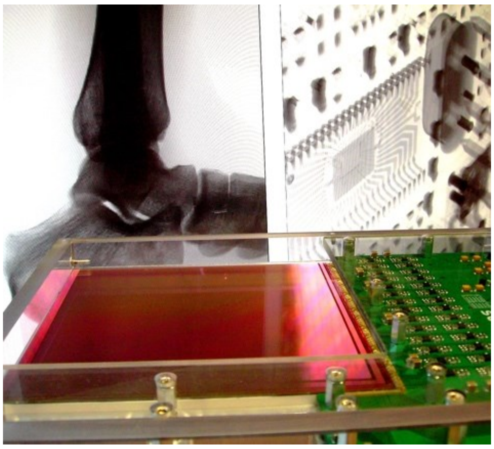
2. Underpinning research (indicative maximum 500 words)

The University of Lincoln led the *EPSRC MI3-Plus* project that, in part, was directed at meeting one of *EPSRC's Grand Challenges in Silicon Technology* (listed in evidence **5.1**) "Large imaging arrays for use in medical applications", and followed on from Prof. Allinson's leadership of the £4.4m *Basic Technology M-I3 - Multidimensional Integrated Intelligent Imaging* consortium. Healthcare requires very large area imagers for many applications (e.g., chest x-rays and mammography) and relatively large pixels (typically 50 – 200 um square as opposed to 1 - 8 um in smartphones and DSLR cameras). Working with *ISDI Ltd* (a start-up enterprise grown out of the earlier *M-I3* work), we tackled the many technical issues that would lead to radiation-hard wafer-scale imagers with a viable commercial yield. Their expertise at detailed CMOS design and access to foundries was coupled with our skills at modelling radiation damage in silicon devices and detailed characterisation, together with our access to a variety of radiation sources and measurement facilities. In association with medical physicists, we defined the specification to meet several medical imaging situations.

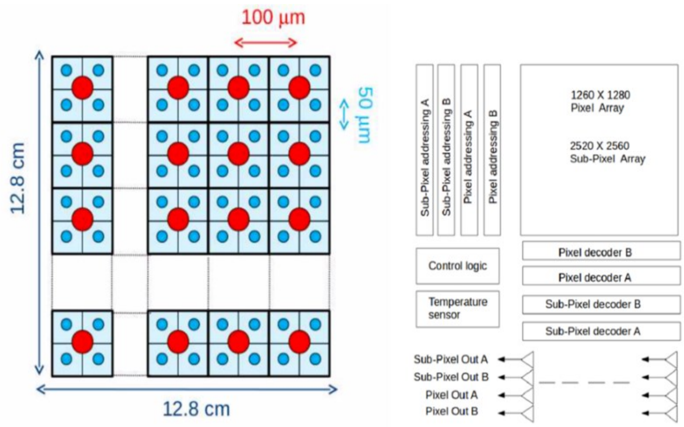
The optical reticule which forms the primary mask for the photolithographic process is only 33 x 26 mm. In x-ray medical imaging, it is not practical to use a lens to focus x-rays, so imagers have to be the same size as the object to be imaged – typically a few tens cm. Silicon wafers are typically 8" in diameter, giving a maximum ~13 cm square imager. The optical reticule cannot be the mask for the whole device as normal but composed of individual building blocks. The wafer is exposed to these different functional blocks using a 2D step-and-repeat process. This process imposes new constraints on the design process and on the design-rules agreed with the foundries. There are up to 30 masks in a full set and these have to registered to each other within a micron as have the individual building blocks.

As mentioned above, medical imagers require non-standard pixel dimensions. Discovering a workable solution necessitated combined modelling work and several test structures and detailed characterisation. The solution was to employ several photodiodes in one effective pixel – in fact, the resulting device, *DynAMITe* (**Dyn**amic range **A**djustable for **M**edical **I**maging **Te**chnology), possessed two different sized pixels in the same array making it effectively two cameras in one. Using multiple photodiodes was a novel concept that simultaneously allowed high- and low-well capacity diodes in the same array. High-well capacity diodes are able to provide high dynamic range, whereas low-well capacity diodes can offer low noise, offering an extended dynamic range when combined. This is important for many medical imaging applications where images are often low contrast on a high background level.

Medical imagers, even when they do not directly detect x-rays, are exposed over their operating life to significant background radiation. Radiation hardness can be drastically increased by careful design layout and suitable choice of the base wafer material and subsequent processing steps. The suitability of a particular structure can only be confirmed through fabricating numbers of test devices – these were characterised by researchers in the *MI-3 Plus* project using specialist radiation sources available to the academic community including the University of Birmingham's MC40 cyclotron.



DynAMITe Imager



DynAMITe Basic Pixel Structure and Architecture

First light tests were conducted in late 2011, with full characterisation and application demonstrators conducted over the following 18 months as evidenced by the cited publications. A second iteration, with new mask set, was fabricated in 2012 to overcome some initial operational shortcomings.

Several of *DynAMITe*'s functions were subsequently incorporated in ISDI's commercial products. DynAMITe was used to illustrate the ability of CMOS imagers to directly record single protons which led to the Lincoln-led *Wellcome Trust* funded project, *PRaVDA (2013-2019)*, to develop the first fully solid-state proton imaging system to provide proton CT to enhance the delivery of Proton Beam Therapy for cancer treatment. In association with ISDI, a new sensor (*Priapus*) was developed for proton imaging. This device is 5 x 10 cm, three-sides buttable, fully radiation-hard and a readout rate in excess of 1,000 frames/sec. We needed the highest possible readout speed to minimise the number of protons per frame to ensure good estimate of proton energies. With one ADC per column (512 in total), this work paved the way for a range of high-speed commercial CMOS imagers.

Work is continuing between ISDI and Lincoln through our EPSRC *OPTIma* project to jointly develop custom read-out devices for silicon strip sensors – these products will form part of ISDI's catalogue.

3. References to the research (indicative maximum of six references)

3.1 Esposito M, Anaxagoras T, Fant A, Wells K, Konstantinidis A, Osmond JP, Evans PM, Speller RD, Allinson NM. DynAMITe: a wafer scale sensor for biomedical applications. Journal of Instrumentation. 2011 Dec 22;6(12):C12064 http://dx.doi.org/10.1088/1748-0221/6/12/C12064

3.2 Konstantinidis AC, Zheng Y, Olivo A, Bliznakova K, Yip M, Anaxagoras T, Wells K, Allinson N, Speller RD. Evaluation of a novel wafer-scale CMOS APS X-ray detector for use in mammography. In 2012 IEEE Nuclear Science Symposium and Medical Imaging Conference Record (NSS/MIC) 2012 Nov 3 (pp. 3254-3260) http://dx.doi.org/10.1109/NSSMIC.2012.6551742

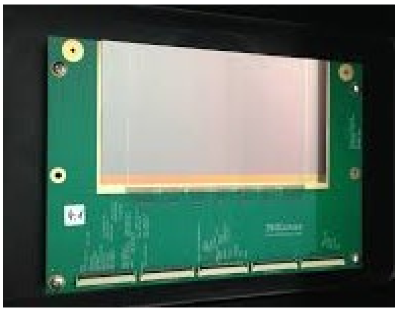
3.3 Esposito M, Anaxagoras T, Larner J, Allinson NM, Wells K. 14C autoradiography with a novel wafer scale CMOS Active Pixel Sensor. Journal of Instrumentation. 2013 Jan 7;8(01):C01011 http://dx.doi.org/10.1088/1748-0221/8/01/C01011

3.4 Poludniowski G, Allinson NM, Anaxagoras T, Esposito M, Green S, Manolopoulos S, Nieto-Camero J, Parker DJ, Price T, Evans PM. Proton-counting radiography for proton therapy: a proof of principle using CMOS APS technology. Physics in Medicine & Biology. 2014 May 1;59(11):2569 http://dx.doi.org/10.1088/0031-9155/59/11/2569

3.5 Esposito M, Anaxagoras T, Evans PM, Green S, Manolopoulos S, Nieto-Camero J, Parker DJ, Poludniowski G, Price T, Waltham C, Allinson NM. CMOS Active Pixel Sensors as energy-range detectors for proton Computed Tomography. Journal of Instrumentation. 2015 Jun 3;10(06):C06001 http://dx.doi.org/10.1088/1748-0221/10/06/C06001

4. Details of the impact (indicative maximum 750 words)

Background context: ISDI Ltd was incorporated July 2010 as a CMOS design house with a focus on scientific, industrial and medical applications. Its original team had a background of working in various national and international research establishments (e.g., *Rutherford Appleton Laboratory, CERN*). *DynAMITe* was the first wafer-scale imager project for the company to produce and to our ambitious specifications. It was a very close partnership as they possessed detailed CMOS design skills and access to silicon foundries and our research data provided user requirements, testing and characterisation of the early designs, access and use of radiation sources, and initial applications in various pre-clinical and clinical domains. During 2011, *ISDI Ltd* formed a partnership with *Dexela Ltd* (04797594), a provider of medical CMOS-based imaging systems who originally used CMOS imagers designed and provided by the Canadian company, *Teledyne DALSA*. Based on our joint progress with *DynAMITe* – improved optical performance, lower noise levels and enhanced radiation-hardness – *Dexela* started to change its provider of imagers to *ISDI Ltd*. *PerkinElmer Inc*. acquired *Dexela* in June 2011. In July 2012, *PerkinElmer* signed an exclusive design and supply agreement with *ISDI Ltd* for all its large area CMOS imagers. *ISDI Ltd* were awarded the *Institution of Engineering and Technology (IET) Innovation Prize for Electronics* (2012) for development of wafer-scale CMOS imagers **[5.2]**).



PRaVDA CMOS Sensor - 10 cm x 5 cm Radiation-hard and 1,000 frames per sec, for direct detection of protons

ISDI IS1512 - 15 cm x 12 cm CMOS Sensor Assembled, with fibre-optic faceplate and CsI scintillators, into 2 x 3 arrays for chest x-ray machines

<u>Impact in the REF period</u>

Significant company growth

ISDI Ltd was started with a £50k revenue stream and has grown organically from audited turnover of to £167k in May 2013 **[5.3]** to over £12m annual turnover in 2020 **[5.4]**). It now fully expects that it can double its revenue over the next 3 to 4 years. *ISDI Ltd* currently directly employs 13 full-time staff and 7 part-time ones, a growth of 16 jobs since 2014. As a result of its growth it has recently moved premises to offer more vertical integration in-house to allow the complete assembly of x-ray imaging products. This allows them to be more price competitive and further optimise their supply chain.

The first large area commercial products from ISDI exploited many of the concepts introduced in *DynAMITe*, for example, selectable pixel size to match different requirements for (say) dental x-rays or mammography. In this way, a single product could address more than one market. In addition, we worked together on optimising 2D stitching of a relatively small reticule (mask) to produce wafer-sized single devices. In particular, curing the "waterfall effect" (a smearing of charge between rows) which led to silicon foundries modifying their design rules.

ISDI Ltd currently has products with pixel sizes ranging from 15 um up to 150 um for the diverse x-ray market. Current catalogue has over 20 models (with detector modules ranging from 6 x 6 cm to 23 x 23 cm active areas) plus variants that cover medical applications (Cone-beam CT, mammography, cephalography, angiography, dental, etc.), industrial non-destructive testing (x-ray imaging), laser positioning and large format photography). The markets for wafer-scale CMOS imagers has widened massively since our original work together for medical radiology – we were a catalysis in promoting the move away from slow *amphorous* flat-panels for mainstream radiography and creating new markets for these versatile imagers.

Dr Ed Bullard, ISDI Chairman, stresses the decisive part that our research played in the company development:

> *ISDI has grown to become one of the leading wafer-scale CMOS image sensor manufacturers globally since beginning its work in this field in the Dynamite project. During this project ISDI designed a novel wafer-scale CMOS image sensor for use in a range of applications including X-ray radiography. The suitability of a particular sensor design to an application such as radiography can only be determined through the fabrication of several test devices which are then build into prototypes, for example prototype X-ray detectors. Several functioning prototypes were manufactured using the novel sensor and were characterised within by researchers in the MI-3 Plus project using specialist radiation sources available to the academic community. This included the University of Birmingham's MC40 cyclotron. The sensor was also characterised in an X-ray detector using an X-ray source for use in multiple medical and industrial applications. The combination of facilities and expertise committed within the MI3 project would not have been available to ISDI without its participation in the project and these resources made an important contribution to the company's subsequent entry into the global X-ray radiography equipment market* **[5.5,** November 2020**]**

This case study is an exemplar of a start-up company collaborating closely with a university research group who were confronting an EPSRC *Grand Challenge* to enable the company to develop into an innovative world-class enterprise.

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1 EPSRC Grand Challenges in Silicon Technology (2008)
https://epsrc.ukri.org/newsevents/pubs/grand-challenges-in-silicon-technology

5.2 Engineering and Technology (IET) Innovation Prize for Electronics (2012) for development of wafer-scale CMOS imagers:
https://eandt.theiet.org/content/articles/2012/11/iet-innovation-awards-winners-announced

5.3 ISDI Accounts May 2013 (from Companies House):
https://beta.companieshouse.gov.uk/company/07314677/filing-history

5.4 ISDI Accounts May 2020 (from Companies House): https://beta.companieshouse.gov.uk/company/07314677/filing-history

5.5 Letter from Dr Edward Bullard, Chairman (2013 to date), ISDI Ltd www.isdicmos.com