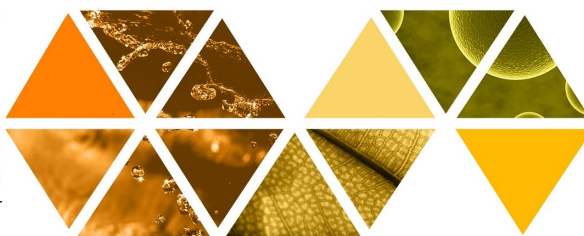




Australian Government  
Australian Research Council

**EI**  
**2018**  
ENGAGEMENT  
AND IMPACT



# Engagement and Impact 2018

**Monash University**

**MON02 (ST) - Impact**

## Overview

### Title

*(Title of the impact study)*

X-ray Phase Contrast Imaging: Applications in Biomedicine and Industrial Materials Characterisation

### Unit of Assessment

02 - Physical Sciences

### Additional FoR codes

*(Identify up to two additional two-digit FoRs that relate to the overall content of the impact study.)*

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### Socio-Economic Objective (SEO) Codes

*(Choose from the list of two-digit SEO codes that are relevant to the impact study.)*

92 - Health

97 - Expanding Knowledge

### Australian and New Zealand Standard Industrial Classification (ANZSIC) Codes

*(Choose from the list of two-digit ANZSIC codes that are relevant to the impact study.)*

69 - Professional, Scientific and Technical Services (Except Computer System Design and Related Services)

81 - Tertiary Education

### Keywords

*(List up to 10 keywords related to the impact described in Part A.)*

X-ray imaging

X-ray phase contrast

Lung imaging

Respiratory diseases

Cystic fibrosis

Neonatal resuscitation

Synchrotron science

Phase reconstruction algorithms

Coherent x-ray optics

Medical and biological imaging

### Sensitivities

Commercially sensitive

No

Culturally sensitive

No

### Sensitivities description

*(Please describe any sensitivities in relation to the impact study that need to be considered, including any particular instructions for ARC staff or assessors, or for the impact study to be made publicly available after EI 2018.)*

### Aboriginal and Torres Strait Islander research flag

*(Is this impact study associated with Aboriginal and Torres Strait Islander content?)*

*NOTE - institutions may identify impact studies where the impact, associated research and/or approach to impact relates to Aboriginal and Torres Strait Islander peoples, nations, communities, language, place, culture and*

knowledges and/or is undertaken with Aboriginal and Torres Strait Islander peoples, nations, and/or communities.)

No

### Science and Research Priorities

*(Does this impact study fall within one or more of the Science and Research Priorities?)*

Yes

Science and Research Priority	Practical Research Challenge
Advanced manufacturing	Specialised, high value-add areas such as high-performance materials, composites, alloys and polymers.
Health	Better models of health care and services that improve outcomes, reduce disparities for disadvantaged and vulnerable groups, increase efficiency and provide greater value for a given expenditure.

# Impact

## Summary of the impact

*(Briefly describe the specific impact in simple, clear English. This will enable the general community to understand the impact of the research.)*

We have made major advances in X-ray imaging by exploiting X-ray phase properties to significantly enhance the visibility of materials that are difficult or impossible to see using conventional imaging modalities. We have developed quantitative tools for measuring changes in the structure and function of complex objects, including biological organs. These technologies are employed worldwide for industrial materials characterisation and biomedical applications, with end users benefiting greatly from our research. Together with our partners we are seeking to cure cystic fibrosis and developing safer methods for the resuscitation of premature infants struggling to breathe at birth. Our discoveries have changed international clinical guidelines, which are saving lives around the world.

## Beneficiaries

*(List up to 10 beneficiaries related to the impact study)*

Premature infants and their families

Clinicians and clinical researchers

Industries including polymer, steel, alloy and food manufacturing

Energy companies exploring fossil fuels

Drug companies

## Countries in which the impact occurred

*(Search the list of countries and add as many as relate to the location of the impact)*

Australia

Netherlands

Spain

Switzerland

Germany

France

Japan

United States of America

China (excludes SARs and Taiwan)

New Zealand

Canada

Russian Federation
England

## Details of the impact

*(Provide a narrative that clearly outlines the research impact. The narrative should explain the relationship between the associated research and the impact. It should also identify the contribution the research has made beyond academia, including:*

- who or what has benefitted from the results of the research (this should identify relevant research end-users, or beneficiaries from industry, the community, government, wider public etc.)*
- the nature or type of impact and how the research made a social, economic, cultural, and/or environmental impact*
- the extent of the impact (with specific references to appropriate evidence, such as cost-benefit-analysis, quantity of those affected, reported benefits etc.)*
- the dates and time period in which the impact occurred.*

*NOTE - the narrative must describe only impact that has occurred within the reference period, and must not make aspirational claims.)*

The imaging techniques and reconstruction algorithms developed by Monash physicists [1-3] have been adopted worldwide at imaging facilities that cater for industrial and biomedical applications.

The “Paganin method” [2] is the ubiquitous gold standard for rapid low-dose three-dimensional X-ray imaging at resolutions down to approximately 100 nm. It is routinely used in hundreds of industrial applications annually (e.g., by the food industry, fossil-fuel industry, polymer industry, chemical industry, steel and alloy industries etc.) It is also applied to numerous clinical studies (lungs, spinal cords, angiography, mammography, neuro-imaging, bone imaging etc.) worldwide, some of which have reached human trials. Many international facilities have developed software packages that incorporate the Paganin method for image reconstruction. These include: ANKPhase; X-TRACT; pyHST2; TomoPy; SYRMEP TomoProject and pyNX. Every major X-ray synchrotron utilises our research, often to a very extensive degree. For example, “99% of the European Synchrotron Radiation Facility’s (ESRF) X-ray micro-tomography beamline ID19 beamtime” utilises the Paganin method, with approximately 20% of beamtime devoted to industrial applications, according to ESRF scientist Dr Alexander Rack. Further, as a cultural impact, the method has revolutionised the study of fossils, which yield astonishing levels of intricate three-dimensional detail when analysed using the Paganin method. The method has impacted in medicine, biology, physics, chemistry, pure mathematics, geology, engineering, manufacturing, food science, energy, archaeology, palaeontology and anthropology. The method has been employed by a number of companies for industrial research, including: Carl Zeiss, Shell, Grace Catalysts Technologies, PSA Peugeot Citroën, 4DX, X-Ray Technologies, Institute for Nuclear Waste Disposal, Nanoscribe GmbH, Sigmatech, Novitom, Unilever, SKF GmbH, Illinois Tool Works, French Atomic Energy and Alternative Energy Agency, etc.

The “single-grid” or “speckle tracking” method of X-ray phase imaging [1], developed at Monash in 2011, is the most recent of just six approaches developed worldwide. This method provides multiple modalities of a moving sample, with each modality sensitive to different properties of the sample. Adopted at all the major synchrotrons, it has already been applied in biomedical research, industry (e.g., fire-retarding foams), metrology and material identification.

Working with A/Prof. Parsons and colleagues from the Women’s and Children’s Hospital (Adelaide), Monash physics researchers have shown the first in vivo measurements of airway surface health at the microscale [5], using our new methods of X-ray imaging [1]. Non-invasive monitoring of airway surface hydration, clearance of inhaled debris, and local lung inflation has provided immediate feedback on the effectiveness of new treatments that target the fatal lung disease associated with cystic fibrosis [5]. Highlighted in The Lancet Respiratory Medicine review paper titled “Remarkable progress toward new treatments for cystic fibrosis”, this ability has led to collaborations with pharmaceutical companies that are working to cure cystic fibrosis, including Parion Sciences, Pharmaxis and Vertex, starting in 2012.

Working with Prof. Hooper’s team of physiologists (Monash University) and clinical researchers from Europe and Australia, our team has investigated strategies to improve lung aeration at birth. Our quantitative imaging techniques demonstrated that a positive end-expiratory pressure (PEEP) is vital to prevent liquid from refilling the airways during expiration and that an initial sustained inflation (SI) was very effective at uniformly aerating the lung [7]. We also showed that surfactant administration with the onset of lung aeration greatly increases the uniformity of lung aeration and that expired CO<sub>2</sub> levels reliably indicate the degree of lung aeration [7]. Videos from these studies are now used as teaching aids to train clinicians world-wide and have prompted a major shift in the

respiratory support devices used in the delivery room. Training programs include the Victorian neonatal resuscitation website - "Neoresus" - and the Swedish neonatal resuscitation training program website (details can be provided on request). The team's published recommendations for safe neonatal resuscitation using PEEP and sustained inflation were respectively included in the 2010 and 2015 International Resuscitation Guidelines [8-9]. In the past 5 years this research has led to 30 published clinical studies/trials world-wide, demonstrating benefit in preterm and term infants, including resource-limited settings, resulting in changes to international resuscitation guidelines world-wide. Examples of clinical trials include those by Foglia et al. (e.g., [10]).

"Stuart Hooper and his group (at Monash) provided excellent animal data on the physiology of neonatal adaptation, which subsequently helped to develop an appropriate approach of supporting neonatal transition after birth."

"... the imaging-based work your team has provided has had a large impact on the current neonatal care we provide in the Netherlands... The imaging studies have completely overturned long held beliefs of how we should resuscitate infants who are compromised at birth. It has been often an eye opener for caregivers when the effect of interventions are explained using your imaging studies... All hospitals now changed over to the use of t-piece resuscitator instead of mask and bag, to guarantee application of PEEP... I am convinced that your work is saving lives."

[Personal correspondence, A/Prof. A.B. te Pas, Pediatrician-Neonatologist (Leiden University Medical Center, the Netherlands)].

## Associated research

*(Briefly describe the research that led to the impact presented for the UoA. The research must meet the definition of research in Section 1.9 of the EI 2018 Submission Guidelines. The description should include details of:*

- what was researched
- when the research occurred
- who conducted the research and what is the association with the institution)

Since 2002 Prof. David Paganin, Dr Marcus Kitchen, Dr Kaye Morgan and other Monash colleagues have together made major advances in X-ray imaging. Their novel techniques utilise phase properties of the X-ray beam to greatly enhance the visibility of those materials that are difficult or even impossible to see using conventional X-ray imaging modalities, including soft tissue [1]. They have developed image reconstruction algorithms that produce quantitative ultra-low-noise images [2, 3]. When combined with computed tomography (CT) for 3D imaging, they showed that the radiation dose can be reduced by factors on the order of thousands via their techniques [4].

In collaboration with A/Prof. Parsons (Women's and Children's Hospital, Adelaide), the team's techniques have been applied to non-invasively image the microscopic airway surface of small animal trachea in studies focused on finding a cure for cystic fibrosis [5].

Working with Prof. Hooper (Monash University), their techniques enabled real-time in vivo measurement of regional lung aeration and alveolar dimensions (see [6]). Together they investigated airway liquid clearance after birth and discovered that it primarily results from pressure differentials caused during inspiration [7]. Since similar pressure gradients can be duplicated with positive pressure ventilation, this provided a new understanding of how resuscitation strategies could better facilitate lung aeration in preterm and term infants.

## FoR of associated research

*(Up to three two-digit FoRs that best describe the associated research)*

02 - Physical Sciences

11 - Medical and Health Sciences

09 - Engineering

## References (up to 10 references, 350 characters per reference)

*(This section should include a list of up to 10 of the most relevant research outputs associated with the impact)*

1. Morgan, K. S., Paganin, D., & Siu, K. K. W. (2012). X-ray phase imaging with a paper analyzer. Applied Physics

2. Paganin, D. M., Mayo, S. C., Gureyev, T. E., Miller, P. R., & Wilkins, S. W. (2002). Simultaneous Phase and Amplitude Extraction from a Single Defocused Image of a Homogeneous Object. *Journal of Microscopy*, 206(1), 33 - 40.

3. Beltran, M. A., Paganin, D., Uesugi, K., & Kitchen, M. J. (2010). 2D and 3D x-ray phase retrieval of multi-material objects using a single defocus distance. *Optics Express*, 18(7), 6423 - 6436. DOI: 10.1364/OE.18.006423

4. Gureyev, T. E., Mayo, S. C., Nesterets, Y., Mohammadi, S., Lockie, D., Menk, R. H., ... Tromba, G. (2014). Investigation of the imaging quality of synchrotron-based phase-contrast mammographic tomography. *Journal of Physics D - Applied Physics*, 47(36), [365401]. DOI: 10.1088/0022-3727/47/36/365401.

5. Morgan, K. S., Donnelley, M., Farrow, N. R., Fouras, A., Yagi, N., Suzuki, Y., ... Parsons, D. (2014). In vivo X-ray imaging reveals improved airway surface hydration after a therapy designed for cystic fibrosis. *American Journal of Respiratory and Critical Care Medicine*, 190(4), 469 - 471. DOI: 10.1164/rccm.201405-0855LE

6. Kitchen, M. J., Lewis, R., Morgan, M. J., Wallace, M. J., Siew, M. L-L., Siu, K. K. W., ... Hooper, S. B. (2008). Dynamic measures of regional lung air volume using phase contrast x-ray imaging. *Physics in Medicine and Biology*, 53(21), 6065 - 6077. DOI: 10.1088/0031-9155/53/21/012

7. Hooper, S., Te Pas, A., & Kitchen, M. (2016). Respiratory transition in the newborn: a three-phase process. *Archives of Disease in Childhood: Fetal and Neonatal Edition*, 101(3), F266-F271. DOI: 10.1136/archdischild-2013-305704

8. Perlman, J. M. et al. (2010). Part 11: Neonatal Resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations, *Circulation*, 122(16) Suppl. 2, S516–S538.

9. Perlman et al., J. M. (2015). Part 7: Neonatal Resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations, *Circulation*, 132(16) Suppl. 1, S204–S241.

10. Foglia, E. E. (2015). Sustained Aeration of Infant Lungs (SAIL) trial: study protocol for a randomized controlled trial. *Trials*, 16(1).

## Additional impact indicator information

### Additional impact indicator information

*(Provide information about any indicators not captured above that are relevant to the impact study, for example return on investment, jobs created, improvements in quality of life years (QALYs). Additional indicators should be quantitative in nature and include:*

- name of indicator (100 characters)*
- data for indicator (200 characters)*
- brief description of indicator and how it is calculated (300 characters).)*