ISRRT Research Fund Application

PART I: SUMMARY OF RESEARCH PROPOSAL

1 (a) Project title: Ultra-low-dose computed tomography in paediatric urolithiasis:

1(b) i). Primary Field: Computed Tomography
Secondary Field: Paediatrics

1(b) ii). A maximum of five keywords to characterize the work of your proposal

Paediatric
Dose reduction
Computed tomography
Urolithiasis
Patient/radiation safety

2. Investigator(s): (Attach CV of each of the investigators)

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Name (First name, Last name)</th>
<th>Email address</th>
<th>Affiliation</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bo Redder Mussmann, Research Radiographer, PhD</td>
<td><a href="mailto:Bo.mussmann@rsyd.dk">Bo.mussmann@rsyd.dk</a></td>
<td>1. Department of Radiology, Odense University Hospital, Denmark</td>
<td>Sdr. Boulevard 29, 5000 Odense C, Denmark</td>
</tr>
<tr>
<td></td>
<td>MaryAnn Hardy, PhD, Professor</td>
<td><a href="mailto:M.L.Hardy1@bradford.ac.uk">M.L.Hardy1@bradford.ac.uk</a></td>
<td>Faculty of Health Studies, University of Bradford, UK</td>
<td>Richmond Road Bradford BD7 1DP United Kingdom</td>
</tr>
<tr>
<td>Co-investigator(s)</td>
<td>Palle Oster, MD, PhD, Professor</td>
<td><a href="mailto:Palle.Joern.Oster@rsyd.dk">Palle.Joern.Oster@rsyd.dk</a></td>
<td>Department of Urology, Hospital Little Belt, Denmark</td>
<td>Sygehusvej 24, 6000 Kolding, Denmark</td>
</tr>
<tr>
<td>Co-investigator(s)</td>
<td>Ole Graumann, MD, Associate professor, PhD.</td>
<td><a href="mailto:Ole.graumann@rsyd.dk">Ole.graumann@rsyd.dk</a></td>
<td>1. Department of Radiology, Odense University Hospital, Denmark</td>
<td>Sdr. Boulevard 29, 5000 Odense C, Denmark</td>
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</table>
3. **Total Allocation Requested [£]: £5000**

4. **Duration of Project:** 24 months

5. **Significance/Outcome of Project:**
   Computed Tomography (CT) is the modality of choice for the diagnosis and evaluation of kidney or ureteric stones. Children with suspected kidney stones are commonly referred for repeat CT examinations to determine size, impact, location and progression of stones over time. As children are more sensitive to radiation exposure compared with adults due to mitotic changes at the cellular level associated with growth, they face an increased risk of developing radiation induced cancers in future years due to longer life expectancy. While the application of the ALARA (As Low As Reasonably Achievable) principle is of paramount importance across all medical imaging examinations, ensuring dose optimisation (lowest dose for desired diagnostic outcome) for paediatric CT examinations is essential, particularly where repeated scans are required to evaluate recurrent disease. However, the evidence base for CT dose optimisation in children is under-developed with best practice and Dose Reference Levels (DRLs) at local, national, and international levels being less well defined than for the comparable adult population, placing one of the most vulnerable patient groups at high risk of inconsistent or poor practice. Using an porcine ex-vivo experimental research design, this study will develop and evaluate an evidence based standardised protocol for ultra-low dose CT in the assessment of paediatric urolithiasis that can be adapted and adopted globally to optimise image acquisition and minimise radiation risk to the child thereby improving practice safety.

6. **Project proposal**
   
   i) **Abstract of research** [limited to ½ page or 250 words, and comprehensible to a non-specialist]:

   **Background:** Computed Tomography (CT) is the imaging modality of choice for assessing renal and ureteric stones in children. Due to the progressive and changing nature of the disease, children suspected of having kidney stones are often referred for repeated CT examinations resulting in a potentially high cumulative radiation dose and increased risk of developing radiation induced cancer. Ultra-Low dose CT technology and post-processing algorithms may provide an opportunity to increase
the safety of CT examinations for the assessment of renal stones in this vulnerable patient group but no study has determined the optimal image acquisition parameters for the clinical application of this technology in children.

**Aim:** To develop and test an ultra-low dose (sub-millisievert) CT protocol capable of visualizing kidney stones of different sizes and chemical compositions within a porcine cadaver to simulate paediatric anatomical composition.

**Method:** Twelve stones of differing size and composition will be surgically inserted into the kidneys, ureters and bladder of a freshly killed porcine specimen. The specimen will be scanned systematically using different technical parameters to achieve an ultra low dose on a single CT scanner. The resultant images/examinations will be assessed independently by 5 radiologists, blinded to the image acquisition parameters, to determine visualization, position and size of the stones. Both intra and inter-observer reliability will be evaluated through random examination presentation and repeated image evaluation.

**Outcome:** The development of an evidence based, optimised ultra-low dose CT examination protocol for the assessment of renal stones in children.

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ii) **The project objectives and long-term impact [maximum 1 page]:** [State the purpose of the proposed investigation, identify the key issues and problems being addressed, and state the possible outcome of the research project in terms of its relevance, significance and value]. [Please list in point form where appropriate]

The primary purpose of this experimental porcine ex-vivo study is to assess the clinical potential of ultra low dose (sub-millisievert) urolithiasis CT examinations in children to reduce the radiation risk burden of repeated CT examinations. This research will be undertaken using a 30kg porcine cadaver to simulate the paediatric body. Currently paediatric abdominal phantoms available for purchase are unsuitable due to inability to insert calculi with the renal and ureteric tract. The diagnostic suitability of the image acquisition protocol will be blindly assessed to determine calculi position and diameter.

The importance of this study reflects a number of professional priorities:

1. Optimising patient diagnosis, follow-up and treatment;
2. Optimising patient radiation dose thereby increasing patient safety;
3. Experimental simulation to evaluate practice changes prior to human evaluation and implementation, thereby reducing experimental risk to child patients;
4. The development of a comprehensive evidence base to support image acquisition techniques and professional ownership of radiographic image acquisition practice across modalities.

The long term benefits of this study are:
1. Primary benefit is the development of an evidence based ultra low-dose CT protocol that could be globally adapted and adopted resulting in potential significant radiation dose reduction and increased patient safety through reduced risk of induced cancer.

2. A significant secondary benefit of the development of this protocol is the reduction in need for patient sedation and anaesthesia due to the relative speed of image acquisition. This again increases patient safety and risk of adverse events as a consequence of sedation.

3. A third benefit to healthcare organisation and patient would be the potential efficiency of adoption of proposed protocol offering opportunities reducing potential time burden on patient and carers if sedation was required, and reducing costs to healthcare providers through greater scan efficiencies and cost savings.

iii) Background/literature review of related work that has been done [maximum 2½ pages, including references]:

The incidence of paediatric urolithiasis has been steadily increasing by 5-10% annually (1) and it is often a recurrent phenomenon (2). Ultrasound (US) is useful if a paediatric patient is suspected of having urolithiasis, but the sensitivity of US is low compared to non-contrast computed tomography (NCCT) (3-8). Therefore, NCCT is often the modality of choice when a patient presents with flank pain even though it may overestimate calculi size by 30 to 50% (9). Several repeated scans may be performed and because paediatric patients are considered at higher risk of developing radiation induced cancer, every effort to reduce radiation dose should be made. Both the initial scan and the follow-up scans are currently performed using a low-dose protocol (i.e. 1 to 3 mSv (10)) capable of detecting calculi and incidental findings. However, if the follow-up scan protocol could be replaced with an ultra-low-dose sub-millisievert protocol without loss of diagnostic confidence the resulting radiation dose may reduce the risk of radiation reduced cancer. In adults dose reductions of up to 90%\(^1\) have been demonstrated without loss of diagnostic image quality using modern iterative reconstruction technique (11-13) and up to 67% in a paediatric tube current simulation study (2). However, the study was performed using a 16-slice scanner without tube-current modulation and without iterative reconstruction, both of which techniques with major radiation dose reduction capability. Thus, a study performed using modern CT technology is required to assess the actual dose saving potential.

\(^1\) Park et al: 90% = 8.31 to 0.68 mSv and unchanged detection of calculi >3mm in a Philips Brilliance scanner
iv) **Research plan and methodology** [maximum 3 pages, including references]:

A porcine specimen mimicking a 7-10 year old child weighing approximately 30 kg will be killed and 12 calculi extracted from patients are surgically inserted in different calyces, the kidney pelvis, in the ureters and in the bladder. The calculi differ in size and material, i.e. calcium oxalate, struvite, uric acid and cystine.

The porcine cadaver will be scanned in a high-end GE Revolution CT scanner (GE Healthcare, Milwaukee, WI, USA) using kV steps between 80 and 120 kVp and iterative reconstruction ranging from 30 to 70%. Prior to the surgical insertion of calculi the attenuation of the porcine tissue will be compared with a representative sample of paediatric abdominal CT scans.

The images will be evaluated by 5 radiologists with different experience who will record the position and diameter of visible calculi and state if the scan is diagnostically acceptable. The radiologists will be blinded to the position, size and number of calculi. Each radiologist’s assessment will be compared with the actual position of the calculi and an inter-observer analysis will be performed.
Contrast-to-Noise Ratio (CNR) between the calculi and surrounding tissue will be measured in each scan.

**Measurements (overview)**
The following measurements are performed in the study:

1. Dose-Length Product (mGy*cm)
2. Noise measured by SD
3. Contrast-to-Noise Ratio
4. Anatomical position of calculi (marked on anatomical sheet)
5. Diameter of calculi (mm)
6. Diagnostical acceptance of scans (yes/no)
7. Inter-observer reliability of image assessments

**Statistical analysis**
The continuous variables will be summarized by descriptive statistics, i.e. mean, standard deviation (SD) and number of observations. Differences between continuous, normally distributed variables will be analysed using parametric tests. Nominal variables are summarized by proportions and the degree of inter-observer agreement is determined using the Fleiss Kappa statistic (14). P-values ≤0.05 will be considered statistically significant.

All analyses are performed using STATA/IC 15.0 (StataCorp. LP, College Station, TX 77845 USA).

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v) **Working schedule** [Describe what will be done under "tasks" and shade the boxes to indicate when the task will be done]

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<th>Tasks</th>
<th>Year 1</th>
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<th>Year 2</th>
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<td>1st Quarter</td>
<td>2nd Quarter</td>
<td>3rd Quarter</td>
<td>4th Quarter</td>
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<td>Research Protocol and literature review</td>
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<td>Planning and coordination of surgery and data acquisition</td>
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<td>Acquiring a porcine specimen</td>
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<td>Surgery and scanning</td>
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<td>Manuscript draft</td>
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<td>Internal review</td>
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<td>Manuscript submission</td>
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<td>Presentation at ISRRRT 2020</td>
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7. i) Allocation requested:

**Total cost of project:**

<table>
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<tr>
<th>Description of items</th>
<th>£</th>
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<tbody>
<tr>
<td>(a) Staff (radiographer, surgeon)</td>
<td>1.000</td>
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<td>(b) Equipment (Porcine specimen, surgical tools)</td>
<td>1.900</td>
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<td>(c) General expenses (publication fee, transport)</td>
<td>1.500</td>
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<td>(d) Conference (Max. £600)</td>
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<tr>
<td><strong>Total amount requested:</strong></td>
<td>5,000 £</td>
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ii) Justifications for allocation

The staff salary is for a specialist radiographer and a surgeon who must perform scans and surgery off-hours. Furthermore, we must invest in at least one porcine specimen for the experiment. Surgical tools used in animals cannot be sterilized and used for human surgery afterwards. Therefore, we cannot borrow tools from the surgical dept. The publishers very often require a substantial fee for publication. In return they offer open access which is an advantage for the dissemination of the research beyond the university context.

8. Supporting documents [List documents submitted in support of this application e.g. support letter for research from institution, ethics approval from Institute Review Board etc.]

1. CV, Bo Mussmann
2. CV, Maryann Hardy
3. CV, Palle Osterh
4. CV, Ole Graumann

9. Research ethics/safety approval:[The primary responsibility of seeking the relevant approval rests with the PI. If human subjects are involved in the research, the respective subject consent form together with the information sheet for subjects should be attached with this proposal.]

Please check the appropriate boxes to confirm if approval for the respective ethics and/or safety issues is required.

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<tr>
<th></th>
<th>Approval not required</th>
<th>Approval obtained</th>
<th>Approval being sought</th>
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<tbody>
<tr>
<td>(i) Human research ethics</td>
<td>x</td>
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<td>(ii) Ionizing radiation safety</td>
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Ethical approval is not required for this research project because all scans are performed on a porcine specimen ex vivo.
10. **Declaration** [Please check the appropriate boxes below and sign the form before submission.]

- I declare that I have not received grant totaling to more than £20,000 in the past 12 months as a principal investigator.

- I confirm that none of the investigators are agents of for-profit, commercial company.

- I confirm that I have been a member of **Radiograf Raadet (Danish Radiographers)** for not less than 2 years.

**OR**

- I confirm that I have been an associate member of the International Society of Radiographers and Radiological Technologists for at least 5 years.

*Signature*: [Signature]

**Name**: Bo Redder Mussmann
- (First name)
- (Middle name)
- (Last name)

**Designation**: Research Radiographer, PhD.

**Institution**: Department of Radiology, Odense University Hospital

**Date**: 30. April 2018

*Please submit electronically to: admin@isrrt.org*
PART II INSTITUTIONAL ENDORSEMENT

[The PI's institution is required to complete this part to certify his/her status in the institution.]

1.a x I confirm that the Principal Investigator Bo R. Mussmann has been a full-time Research Radiographer of this institution since 1 December 2011.

OR

1.b ☐ I confirm that the Principal Investigator ______________________(name) will be a full-time / part-time* ______________________(position of Principal Investigator) of this institution starting _________________(date).

2. Our institution Odense University Hospital, Dept. of Radiology will fully support the conduct of the proposed project if the application is successful.

Signature :

Name : Jens Karstoft, MD, PhD.

Designation : Head of Department

Institution : Department of Radiology, Odense University Hospital

Date : 30/4/18