Combining cycloidal computed tomography with machine learning: a mechanism to disrupt the costly relationship between spatial resolution and radiation dose (ML-CYCLO-CT)

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ABSTRACT
A novel imaging concept ("cycloidal computed tomography") was combined with convolutional neural network (CNN) based data recovery. The experimental method consists in using a structured x-ray beam and applying cycloidal sampling by which the sample is simultaneously rotated and translated. The scanner layout results in an increase in spatial resolution while ensuring that parts of the sample are shielded from radiation, and the "roto-translation" sampling allows for rapid scanning. The application of a Mixed-Scale Dense CNN enables the reconstruction of high-resolution images from highly incomplete data, the latter corresponding to a substantial reduction in the delivered radiation dose.

Keywords: 3D imaging; x-rays; computed tomography; machine learning; convolutional neural networks.

1. INTRODUCTION

X-ray computed tomography (CT) is essential in medicine, but it has also emerged as a key tool for the non-destructive characterization of samples in biomedical research and numerous other disciplines. A strength of this imaging technique is that it can provide spatial resolutions ranging from the mm down to the nm scale. However, increasing the spatial resolution in a CT slice is typically associated with a quadratic increase of the delivered radiation dose, at least if no loss in the signal-to-noise ratio (SNR) should be suffered[1]. This is problematic when scanning dose-sensitive samples and performing in vivo studies.

Cycloidal computed tomography (cyclo-CT) is a novel imaging concept that was developed in an effort to solve this issue. The central idea is to employ a mask to structure the x-ray beam into an array of narrow beamlets, and to apply a cycloidal sampling scheme by which the sample is simultaneously rotated and translated (see Fig. 1A). This unique combination of scanner layout and acquisition strategy provides access to high-frequency information while at the same time cutting down on the delivered radiation dose[2].

As a result of this dose saving, cyclo-CT data are however highly incomplete (see Fig 1B) and the missing data need to be restored before high-resolution CT images can be reconstructed. In this ATTRACT project, we have investigated the merits of exploiting new directions in machine learning (ML) for this purpose. Specifically, we have applied the recently proposed Mixed-Scale Dense (MSD) convolutional neural network (CNN) architecture[3,4] to recover complete sinograms from incomplete cycloidal datasets. Our results show that high-resolution CT images can be obtained using only a fraction of the dose conventionally deemed necessary without encountering a significant loss in image quality. It was also shown that the MSD CNN outperforms a previously used data recovery approach (bicubic interpolation). An easy-to-implement strategy for acquiring data to train the network has been proposed; this method is very general and does not rely on previously acquired images of similar samples. Looking forward, we believe that, in combination, cyclo-CT and ML based data recovery bear great potential to increase the application range of CT by providing a high spatial resolution and overall image quality while allowing to perform scans at a much lower radiation dose.

2. STATE OF THE ART

Progress in many biomedical research areas is currently held back by a lack of a fast, accessible and non-destructive imaging technology that can provide 3D images with microscale spatial resolution. Traditional methods such as histology and electron microscopy possess the necessary spatial resolution capabilities, but they require that the sample is destroyed in preparation for being scanned (through slicing, sectioning and/or staining), and images are inherently 2D; where extensions to 3D exist, these are extremely time consuming. Therefore, these methods are not suited for longitudinal or

in vivo studies, and can only be used to investigate relatively small tissue sections[5].

High-resolution CT has emerged as a possible solution, owing to its ability to provide 3D images non-destructively[6]. Yet, the fact that samples are exposed to high doses of ionising radiation remains to be a significant drawback, to an extent that inspections of dose-sensitive samples, such as specimens involving live cell cultures, or small animals, are severely restricted. Cyclo-CT has a demonstrated potential to substantially relax the dose-penalty of increasing spatial resolution[2], but image reconstruction relies on the recovery of complete sinograms from highly incomplete measurement data. The performance of this recovery step critically affects the image quality that can be achieved; therefore, it is essential that this step is continuously optimised.

Machine learning techniques have seen a surge in their application in the context of CT. CNNs have been applied as part of the tomographic image reconstruction process[7,8], thereby improving the reconstruction quality, or as a post-processing tool to improve the quality of CT images after they have been reconstructed[4,9]. Existing CNNs often require extensive computer memory and large amounts of training data (e.g. up to thousands of images) to produce accurate results. The MSD CNN architecture that was applied in this ATTRACT project differs from popular existing CNNs by using dilated convolutions instead of scaling operations to capture image features at different scales, and by connecting all network layers with each other. As a result, MSD networks typically require fewer intermediate images and learned parameters to achieve accurate results compared with existing CNNs, and are therefore well-suited for efficiently processing large datasets and accurately learning from relatively few training images. It has recently been demonstrated that the MSD CNN can substantially improve the quality of images reconstructed from CT measurements that were noisy and/or incomplete due to angular under-sampling[4].

3. BREAKTHROUGH CHARACTER OF THE PROJECT

The objective of this project was to generate high-quality, high-resolution images at a substantially reduced radiation dose by applying the MSD CNN to the data recovery problem in cyclo-CT. The breakthrough character of this ambition is evident; low-dose, high-resolution scanning opens up many new applications, especially in the biomedical field where samples are often dose sensitive. For example, significant advantages could be gained in pre-clinical imaging, where currently longitudinal small animal studies are severely restricted by dose constraints. As well as potentially reducing the number of animals required in research, the ability to perform repeated scans on the same animal would remove the issue of "inter-subject variability", with potentially transformative implications for drug development. Other examples of applications that can become possible through our method are provided in Section 5.3.

Besides making high-resolution imaging possible at a lower radiation dose, the cyclo-CT method has additional advantages that feed into the breakthrough character of this project. Besides an excessive dose delivery, several other concerns typically hamper the ability to increase spatial resolution in CT. For example, this can only be done with specialized scanner hardware[1,10] (i.e. x-ray sources with adequately small focal spots and detectors with appropriately small pixels), which is an inflexible constraint. Cyclo-CT, due to the structured x-ray beam, enables disrupting this restrictive relationship between the spatial resolution and the blurring due to an extended focal spot size and the detector's spatial response[11,12]. This has an important consequence: higher (and tuneable) spatial resolution in CT becomes accessible with systems that traditionally would not allow it, and including with much larger fields of view, which may allow for the development of significantly cheaper systems without having to compromise spatial resolution and, more generally, image quality.

4. PROJECT RESULTS

An initial project aim was to develop an easy-to-implement strategy for the acquisition of training data for the MSD CNN. To avoid having to scan many samples of the same type at a high resolution and using these images to train the network, in our approach training data are acquired as part of the scan of each individual sample. Specifically, the acquisition of a few high-resolution projections is integrated into a cycloidal scan (see Fig. 1C); these projections are then used to train the network, which is subsequently applied to recover the missing entries in all other projections.

We have run several tests (including both simulated and experimental scans) to demonstrate the merit of applying the MSD CNN to the data recovery problem in cyclo-CT. Here we report on experimental scans of a formalin-fixed chicken bone placed in a plastic container of approximately 9 mm diameter. For a proof-of-concept, we acquired a complete, high-resolution dataset that was subsequently sub-sampled in an interleaved fashion (see Fig. 1B) so as to mimic cycloidal acquisitions. Every 10th projection was kept complete (90 projections in total). A 100-layer MSD network was trained with bicubic interpolated cycloidal sinograms as network input and the complete projections as training target. Out of 300 available sinograms (obtained for 300 cross-sections of the scanned sample), 270 were used for training, while the remaining 30 were used as a validation set to monitor performance. After training, the MSD CNN was applied to the remaining cycloidally sampled projections so as to

restore the missing entries in these. Once a complete sinogram had been recovered, image reconstruction was performed with filtered back projection (FBP). For comparison, we have reprocessed the data using bicubic interpolation as the data recovery method.

The results are shown in Fig. 1D. The left panel shows the image reconstructed from complete (i.e. high dose) data, the central panel shows the cycloidal image reconstructed with bicubic interpolation, and the right panel shows the cycloidal image reconstructed with the MSD CNN. It can be seen that the spatial resolution in both cycloidal images is comparable to that in the high-dose image, but that the application of the MSD CNN leads to a better overall image quality than bicubic interpolation. Notably, both cycloidal images were reconstructed from 22% of the data (i.e. using only 22% of the dose).

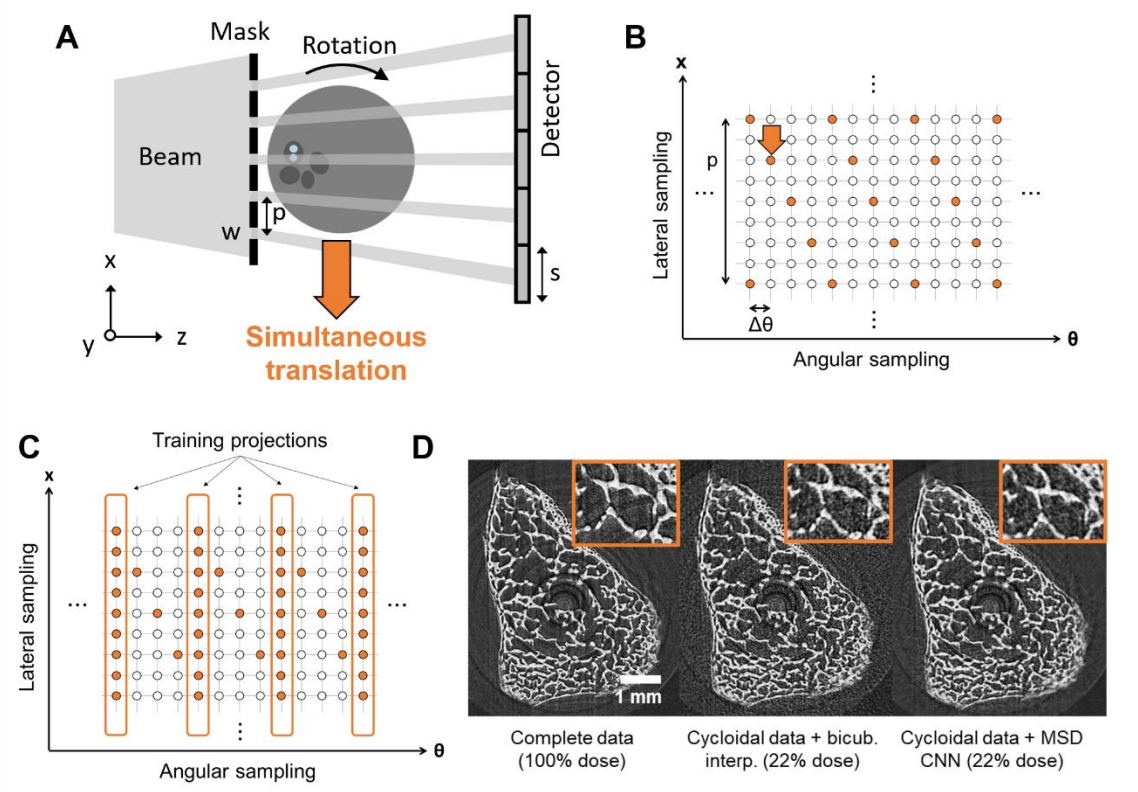

Figure 1. A) Schematic of a cyclo-CT setup; a mask in front of the sample splits the beam into an array of separated beamlets; provided the mask apertures are smaller than the blur of the x-ray source and the detector combined, this configuration leads to the presence of higher spatial frequencies in the image formation process[2,11,12], facilitating high-resolution imaging; the sample is simultaneously rotated and translated during a scan, which corresponds to a cycloidal sampling motion. B) Sampling grid for a cycloidal acquisition; the acquired data points are shown in orange, the missing data points are marked by the empty circles; the data are highly incomplete, but the cycloidal sample motion creates an interleaved sampling pattern which has been shown to ease the challenge of recovering the missing data points via mathematical methods. C) Sampling grid for ML-cyclo-CT scans; the acquisition of complete training projections is integrated into a cycloidal scan. D) Project results obtained for a chicken bone; images were reconstructed from complete data (100% dose) and cycloidal data (22% dose) respectively; the performances at completing the dataset of bicubic interpolation and the MSD CNN can be compared.

5. FUTURE PROJECT VISION

5.1. Technology Scaling

Scaling up the cyclo-CT idea will be underpinned by the effective development of dedicated collimators with alternating transmitting and absorbing septa, which shield the sample from large amounts of radiation while simultaneously providing access to higher spatial frequencies than what would be permitted by the source and detector blur[11,12]. In technology terms, the project outcomes can be realised either through the development of new, standalone imaging systems as well as by possibly retrofitting existing scanners with appropriately designed masks. Both solutions would be supported by a dedicated software package implementing ML-based data recovery and tomographic image reconstruction. We will likely build on existing collaborations with companies in the x-ray and micro-CT domain to advance cyclo-CT to TRL 5-7 and ultimately into an industrial product.

5.2. Project Synergies and Outreach

We will seek to combine our project outcomes with the outcomes from other ATTRACT projects, specifically those that also deal with x-ray imaging. Besides those x-ray imaging projects either led by our group at UCL or where UCL is a partner, we believe that other ATTRACT projects focused on innovative CT reconstruction methods could have great potential for being joined with our approach. In order to strengthen the EU research infrastructure, we will also seek to build on the strong links we have with several European synchrotrons and invite these to join our consortium as appropriate.

5.3. Technology application and demonstration cases

Our overarching vision is to develop a new high-resolution CT system for application in the biomedical sciences. We would like to mention tissue engineering, a discipline targeted at developing “lab-grown” transplant organs, as a specific example. Tissue engineering is particularly affected by the severe dose delivery of conventional high-resolution CT imaging approaches, as it relies heavily on samples with live cell cultures, and animal models. The fact that, with cyclo-CT, high-resolution scanning no longer involves the delivery of such excessive doses will enable repeated imaging of such samples and allow studying cell migration in 4D, which is not possible with current technology. Likewise, our device will provide a detailed understanding of the in vivo performance of engineered tissue, as samples can be monitored longitudinally at high resolution following their implantation into mice. We collaborate with world-leading tissue engineers and therefore avail of guidance from the envisaged users of our technology. In the long term, we believe that the development of a new high-resolution CT system based on cyclo-CT combined with machine learning can lead to the development of new medical treatments, which will be of tremendous benefit to European society. In terms of advancing the EU research infrastructure, our approach is expected to provide new scanning opportunities that can be made accessible to the wider scientific community. Although we are initially envisaging to develop a CT machine for use in biomedical research labs, the concepts that underpin the technology may equally be implemented at synchrotrons. This is desirable as it would widen the current scope of biomedical beamlines (due to the envisaged large dose savings of high-resolution scans) and allow their worldwide user community to tackle scientific problems currently practically inaccessible, for instance the repeated tomographic imaging of cell-bearing biomaterials, or in vivo studies in general.

5.4. Technology commercialization

We expect that our ongoing work within the project remit will lead to commercially exploitable results, and the development of a commercial product is a key ambition of ours. As described above, commercialisation could take place in the form of an add-on for performing ML-based cyclo-CT that can be seamlessly integrated into existing CT scanners; or as a new, standalone imaging device. We will explore both avenues together with suitable industrial partners. Due to our existing relationships, we would not strictly be reliant upon securing additional investment in our technology; however, we would review opportunities should these arise.

5.5. Envisioned risks

Our vision to develop a new CT scanning technology for biomedical research that can overcome current hurdles such as the delivery of high doses of radiation is certainly ambitious and involves overcoming several scientific challenges. Perhaps the most critical challenge (and the corresponding risk that this cannot be achieved) is to obtain high enough image contrast to visualise biological structures which are often faint due to their weak intrinsic ability to attenuate x-rays. Should this not be the case, we would build a cyclo-CT system with an option to switch from attenuation into phase contrast mode. Previous work has shown the feasibility of this plan[2]; e.g. by adding a second custom-designed collimator (mask) in front of the detector, the imaging system is effectively turned into an edge illumination x-ray phase contrast device that can sense x-ray refraction alongside attenuation[13]. Studies have demonstrated the ability of

refraction/phase contrast to lead to a better feature detectability where attenuation contrast fails[14-16].

5.6. Liaison with Student Teams and Socio-Economic Study

Our group has a long-standing track record of engaging with members of the public at all ages to communicate the importance of our work and we would continue doing so as part of ATTRACT Phase 2. The preparation of explanatory slides to introduce the project and show the results at a level appropriate for MSc students would become a core element of our student engagement strategy. We would contribute to the expert-driven socio-economic study of the ATTRACT initiative and ecosystem through interviews as well as technology impact references.

6. ACKNOWLEDGEMENT

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