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12th February 2021

Dear ACFRT Board of Trustees,

Please accept this letter as documentation of our annual report for the "*Detailed characterisation of Structure-Function Relationships in Mild Cystic Fibrosis Lung Disease and validation of an ultra-low dose high resolution computerised tomography (HRCT) scanning protocol*", for which we received a ACFRT Innovation Grant in 2018. Thank you again for supporting our study.

In brief our study focused on providing critical information to guide future screening protocols aimed at early detection of CF related lung disease. We aimed to use the most sensitive outcome measures for the detection of both structural and functional changes in those with mild disease and to significantly reduce the radiation dose associated with a high resolution CT scan. Importantly this work will be transferable to other CF centers internationally since the tools are widely available.

Aims and Objectives

- Provide detailed characterisation of structure-function relationships in children with mild CF lung disease in both late preschool and school-aged children.
- Describe the functional impact of early changes and relationships to other key CF outcomes (e.g. pulmonary exacerbation rates, progression of MBW since the preschool age range).
- Explore the feasibility and utility of ultra-low dose HRCT scanning protocols in this setting.

From the tables below we hope we are able to provide sufficient feedback that we achieved our recruitment target, the data collection for the study is completed and we are in the final stages of writing up for publication. We hope that this pilot study will provide a basis for use of these outcome measures in both a larger study but also in some cases clinical practice. We aim to present and disseminate these findings at both national and international conferences as well as publish the results in a relevant high impact journal.

Thank you again for supporting our project.

Yours Sincerely



A/Prof Paul D Robinson & Dr Katie J Bayfield
Clinical Associate Professor/Staff Specialist & Research
Officer



Detailed timeline – Key dates

Date and Activity	Details and output
September 2020	The study was displayed and presented as a poster at the local Westmead showcase, showing research within the SCHN network.
October 2020 – NACFC Nashville	We had meetings with collaborators at this conference to discuss progress so far and potential expansion of data analysis.
January 2020	No CT's were able to be completed due to hospital downtime.
January 2020	Subset of children completed oxygen enhanced MRI scans. The children who we were able to train and test for this scan are the youngest to do so to date. We were able to compare routine fixed breathing as well as free breathing during the scans; this should make future scanning easier for all sites.
April/May 2020	Pause in recruitment due to the COVID 19 Global pandemic – 47 recruited to date.
8-9 Sept 2020 – Virtual European Respiratory Society Conference	The project entitled “Use of ultra-low dose CT does not impact structure-function relationships in early Cystic Fibrosis lung disease” was presented in the “New frontiers in cystic fibrosis imaging and lung physiology” virtual session. The information was received well and interesting questions posed.
21/09/2020	Final patient recruited to the study: 57 (n=50 final dataset).
21 OCT 2020 – Virtual NACFC Conference	“Ultra-low dose CT does not impact structure-function relationships in early Cystic Fibrosis lung disease” was pre recorded and presented as an e-poster at this virtual conference.
Results and Conclusions	<p>Sensitive surrogate outcome measures for both structural and functional measures are required, especially for those with early Cystic Fibrosis lung disease where lifetime radiation exposure may increase with increased life expectancy and traditional lung function tools miss very early abnormality.</p> <p>Ultra-low dose imaging protocols preserved sensitivity and structure-function relationships compared to standard dose CT at a significantly lower radiation dose. The most sensitive markers of early lung disease were CT air trapping; LCI and MBW assessed gas trapping.</p> <p>Ultra low dose CT protocols and multiple breath washout provide complementary information and offer exciting utility to better understand the pathogenesis and evolution of early CF lung disease.</p>

List of Outcomes

Oral Presentations

1. Bayfield, K.J., Robinson, P.D., *et al.* Characterisation of Structure Function Relationships in Mild Cystic Fibrosis Lung Disease presented at the Australian CF Conference 2019.
2. Bayfield, K., *et al.* (2020). "Late Breaking Abstract - Use of ultra-low dose CT does not impact structure-function relationships in early Cystic Fibrosis lung disease." ERS Virtual Conference September 2020.

Abstracts

1. Bayfield K.J., Robinson, P.D., *et al.* Characterisation of Structure Function Relationships in Mild Cystic Fibrosis Lung Disease for presentation at the Thoracic Society and Society of Respiratory Science of Australia and New Zealand (TSANZSRS) Conference in March 2020.



2. Bayfield, K., et al. (2020). "Late Breaking Abstract - Use of ultra-low dose CT does not impact structure-function relationships in early Cystic Fibrosis lung disease." *European Respiratory Journal* 56(suppl 64): 4310. ERS Virtual Conference September 2020.
3. Bayfield, K. J., Weinheimer, O, Boyton, C, Fitzpatrick, R, Middleton, A, Kennedy, B, Blaxland, A, Jayasuriya, G, Caplain, N, Wielputz, M.O, Yu, L, Galban, C.J, Robinson, T.E, Bartholmai, B, Gustafsson, P, Fitzgerald, D, Selvadurai, H, & Robinson, P.D. (2020). "Ultra-low dose CT does not impact structure-function relationships in early Cystic Fibrosis lung disease." *Pediatric Pulmonology* 55(S2): 291-292. NACFC Virtual Conference October 2020

Upcoming outcomes

1. TSANZ 2021 Conference - oral presentation
2. ATS 2021 Conference
3. We look forward to presenting this data at the 2021 Australian CF conference

Upcoming papers

We are in the final stages of drafting and finalizing our main paper with collaborators from the study. We envisage there will be a series of papers from the results we have generated.

Legacy and Follow-up

We are in the process of sourcing funding for the follow up of these children, using the techniques that were refined and utilized within this study. The innovative methodologies have changed and influenced practice and we hope follow-on studies will upscale the results and reach for CF patients.

