

Title	Radiologic imaging in cystic fibrosis: cumulative effective dose and changing trends over 2 decades
Author(s)	O'Connell, Oisín J.; McWilliams, Sebastian R.; McGarrigle, AnneMarie; O'Connor, Owen J.; Shanahan, Fergus; Mullane, David; Eustace, Joseph; Maher, Michael M.; Plant, Barry J.
Publication date	2015-12-16
Original citation	O'Connell, O. J., McWilliams, S., McGarrigle, A., O'Connor, O. J., Shanahan, F., Mullane, D., Eustace, J., Maher, M. M. and Plant, B. J. (2012) 'Radiologic Imaging in Cystic Fibrosis: Cumulative Effective Dose and Changing Trends Over 2 Decades', Chest, 141(6), pp. 1575-1583. doi: 10.1378/chest.11-1972
Type of publication	Article (peer-reviewed)
Link to publisher's version	http://www.sciencedirect.com/science/article/pii/S0012369212603481 http://dx.doi.org/10.1378/chest.11-1972 Access to the full text of the published version may require a subscription.
Rights	© 2012 American College of Chest Physicians. Published by Elsevier. This accepted manuscript version is made available under the CC-BY-NC-ND 4.0 license. http://creativecommons.org/licenses/by-nc-nd/4.0/
Item downloaded from	http://hdl.handle.net/10468/6613

Downloaded on 2018-08-23T17:53:51Z

CHEST[®]

Official publication of the American College of Chest Physicians



Radiological imaging in cystic fibrosis: cumulative effective dose & changing trends over 2 decades

O. J. O'Connell, S. McWilliams, A. M. McGarrigle, O. J. O'Connor, F. Shanahan,
D. Mullane, J. Eustace, M. M. Maher and B. J. Plant

Chest, Prepublished online December 29, 2011;
DOI 10.1378/chest.11-1972

The online version of this article, along with updated information and services
can be found online on the World Wide Web at:
<http://chestjournal.chestpubs.org/content/early/2011/12/28/chest.11-1972>

Chest is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 2011 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook, IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder.
(<http://chestjournal.chestpubs.org/site/misc/reprints.xhtml>) ISSN:0012-3692

CHEST Papers in Press are peer-reviewed, accepted articles that have not yet been published in an issue of the journal and have not yet been edited or typeset. The final version may contain substantive or nonsubstantive changes. These articles are indexed by PubMed, but any references to an in-press article must include the digital object identifier (DOI) and date of in-press publication.

CHEST Papers in Press are not under media or public embargo once they appear online. For inquiries, please contact the AACP Media Relations Department at (847) 498-1400 or media@chestnet.org.

A M E R I C A N C O L L E G E O F



P H Y S I C I A N S[®]

1 **Word Count Abstract: 253**

2 **Word Count Text: 3655**

3

4 **Title: Radiological imaging in cystic fibrosis: cumulative effective dose &**

5 **changing trends over 2 decades.**

6 **Running Header: Iatrogenic Radiation exposure in patients with CF.**

7 **Authors:**

- 8 1. O'Connell OJ, MD, Cork Cystic Fibrosis Center, Cork University Hospital, University
9 College Cork, Cork.
- 10 2. McWilliams S, MD, Cork Cystic Fibrosis Center, Cork University Hospital, University
11 College Cork, Cork.
- 12 3. McGarrigle AM, PhD, Dept. of Radiation Physics, Cork University Hospital, University
13 College Cork, Cork.
- 14 4. O'Connor OJ, MD, Dept. of Radiology, Cork University Hospital, University College Cork,
15 Cork.
- 16 5. Shanahan F, MD, BSc, FRCPI, FRCP (UK), FACP, FRCP(C), Dept. of Medicine, Cork
17 University Hospital, University College Cork, Cork.
- 18 6. Mullane D, MD, Cork Cystic Fibrosis Center, Cork University Hospital, University College
19 Cork, Cork.
- 20 7. Eustace J, MB, MRCPI, MHS, MD, Dept. of Renal Medicine, Cork University Hospital,
21 University College Cork, Cork.
- 22 8. Maher MM, MD, FRCSI, FFR RCSI, FRCR, Dept. of Radiology, Cork University Hospital,
23 University College Cork, Cork.
- 24 9. Plant BJ, MRCPI, MFSEM, MD, Cork Cystic Fibrosis Center, Cork University Hospital,
25 University College Cork, Cork.

26

27 **Guarantor:** Dr Barry Plant, Consultant Pulmonologist,
28 Director of Cork Adult Cystic Fibrosis Center,
29 Cork University Hospital,
30 University College Cork,
31 Cork.
32 Ireland.

33 Barry.Plant@hse.ie

34

35 **Study Design:** OJOC, SMcW, OJOC, DM, MMM, BJP

36 **Statistical Analysis:** SMcW, JE

37 **Manuscript preparation:** OJOC, AMcG, FS, MMM, BJP

38

39

1 **Abstract**

2 **Objective:**

3 With the increasing life expectancy for patients with cystic fibrosis (CF), and a known
4 predisposition to certain cancers, cumulative radiation exposure from radiological imaging is of
5 increasing significance. This study explores the estimated cumulative effective radiation dose
6 over a 17 year period from radiological procedures, and changing trends of imaging modalities
7 over this period.

8 **Methods:** Estimated cumulative effective dose (CED) from all thoracic and extra-thoracic
9 imaging modalities and interventional radiology procedures for both adult and pediatric CF
10 patients, exclusively attending a nationally designated CF center between 1992-2009 for
11 >1year, was determined. The study period was divided into 3 equal tertiles and estimated CED
12 attributable to all radiological procedures was estimated for each tertile.

13 **Results:** 230 patients met inclusion criteria (2,240 person-years of follow-up; 5596 radiological
14 procedures). CED was >75mSv for 1 patient (0.43%), 36 patients (15.6%) had a CED between 20-
15 75mSv, 56 patients (24.3%) had a CED between 5-20mSv and in 138 patients (60%) the CED was
16 estimated to be between 0-5mSv over the study period. The mean annual CED/patient
17 increased consecutively from 0.39mSv/yr to 0.47mSv/yr to 1.67mSv/yr, over the tertiles 1-3 of
18 the study period respectively ($p<0.001$). Thoracic imaging accounted for 46.9% of the total CED
19 and abdomino-pelvic imaging accounted for 42.9% of the CED respectively. There was an
20 associated 5.9 fold increase in the use of all CT scanning per patient ($p<0.001$).

1 **Conclusion:** This study highlights the increasing exposure to ionizing radiation to CF patients as
2 a result of diagnostic imaging, primarily attributable to CT scanning. Increased awareness of
3 CED and strategies to reduce this exposure are needed.

4 **MeSH Terms (3-5):** Cystic Fibrosis [C08.381.187], Radiation Dosage [N06.850.810.250],
5 Diagnostic Imaging [E01.370.350]

6 **Introduction:**

7 Experimental and epidemiological evidence has linked the cumulative exposure to ionizing
8 radiation, even at low doses, with an age-dependent increased risk for the development of
9 malignancy¹⁻⁴. A number of recent studies have highlighted the issue of cumulative radiation
10 exposure towards hospitalized patients^{2,3}. However, few studies have addressed this issue in
11 patients with chronic diseases and there are no studies to date quantifying the annual
12 cumulative exposure to ionizing radiation incurred as a result of diagnostic and interventional
13 radiology procedures for patients with cystic fibrosis (CF). With the progressive improvements
14 in life expectancy for patients with CF, the cumulative exposure to ionizing radiation
15 attributable to diagnostic imaging and interventional radiology procedures is of increasing
16 significance⁵⁻⁷.

17 A number of recent studies have highlighted that CF patients have an increased standardized
18 incidence ratio (SIR; the ratio of the observed to the expected number of cancers in the cohort)
19 of developing a large number of malignancies, with notable increases in the SIR for thoracic
20 cancers, cancers of the digestive tract (SIR 5.6), kidney (SIR 14.0), thyroid (SIR 9.8) and
21 lymphoma (SIR 7.3)⁸. The issue of exposure to ionizing radiation in the diagnostic range in this

1 cohort raises additional concerns. Linking the exposure of iatrogenic ionizing radiation to
2 malignancy is controversial, however data within the general population has approximately
3 linked each 10 millisieverts (mSv) of radiation exposure to an incremental mean increase risk in
4 cancer of 1 radiation induced malignancy per 1000 patients, although this risk is significantly
5 affected by both age of exposure and gender⁹⁻¹⁰. Secondly, previous studies have proposed
6 that additional caution is required in patient sub-groups (e.g. Crohn's disease patients) who
7 because of their chronic relapsing illnesses require repeated diagnostic imaging throughout
8 their lifetime and who already have an increased lifetime risk of developing cancer, may suffer
9 as a result of possible synergy between these two factors resulting in an ever higher incidence
10 of developing cancer¹¹.

11 The benefits of radiological imaging are well proven and have been comprehensively
12 characterized for CF patients¹²⁻¹⁴. In CF patients, thoracic CT can detect lung changes from early
13 infancy and before they become apparent by pulmonary function testing¹⁵⁻¹⁶. An increasing
14 number of clinical trials are using thoracic CT scores as surrogate end points in their studies¹⁷⁻
15¹⁸. Additionally, some centers use high resolution CT in the routine monitoring of disease
16 progression for pediatric patients with CF¹⁹.

17 This is the first study to examine the cumulative effective radiation dose (CED) incurred by a
18 cohort of adult and pediatric patients with CF, and the changing trends in use of radiological
19 imaging modalities in this cohort, over 17 years. It is also the first study to characterize relative
20 anatomical radiation distribution including the percentage of cumulative exposure arising from

1 thoracic and abdomino-pelvic imaging and the relationship between clinical phenotype and
2 CED.

3 **Methods:**

4 **Study Population:**

5 All pediatric and adult patients with CF who exclusively attended a nationally designated Adult
6 or Pediatric CF center , for all medical therapy for > 1year from the 1st July 1992 to the time of
7 lung transplantation, hospital treatment transfer or death until the study end date of 1st May,
8 2009 were included in this study. Ethical approval for the study was granted by the institution's
9 research ethics committee. Approval number (reference number) for this study: ECM
10 4(z)03/03/09. All demographic, clinical data and hospital attendances were obtained by chart
11 review. Lung function was measured in accordance with the standards set out by the European
12 Respiratory Society and recorded as maximum annual FEV₁% predicted using the European
13 Community for Coal and Steel (ECCS) reference values²⁰.

14 **Data Source:**

15 Details of all imaging studies and interventional radiology procedures performed on adult
16 (>18yrs) and pediatric (<18yrs) patients in the study cohort over the 17 year study period 1st
17 July 1992 to 1st May 2009 were obtained from the computerized radiology information system
18 of the radiology department. All studies were requested for clinical purposes only, by
19 experienced hospital clinicians, predominantly by attending pediatricians and attending
20 pulmonologists with a special interest in cystic fibrosis. The CED was measured in millisieverts
21 (mSv), a measure designed to represent the overall detrimental effect of a non-uniform ionizing

1 radiation exposure and useful for population-level comparisons across different types of
2 radiation exposure²¹. As per previous studies^{11 22}, estimations were based on a recent article
3 by Mettler et al, which provided a compilation of the mean effective doses for radiological and
4 nuclear medicine examinations from the recent published literature, across the USA, Canada,
5 Japan, Australia and Western Europe, over a similar time period as this study²³. In
6 circumstances where this source was insufficient, estimates were calculated from other
7 published sources or extrapolated from doses reported for similar procedures relevant to our
8 studied population over a similar time period and using similar dose calculation methodology²⁴.
9 CED was determined for general radiography (Gen), computed tomography (CT), general
10 interventional procedures (GIV), nuclear medicine (NM), fluoroscopy (Fl) including all barium
11 examinations (Ba), and data were then subcategorized into the anatomical area imaged as
12 thoracic, abdomino-pelvic and other. All computed tomography (CT) scans during the study
13 period (1992-2009) were performed using either an incremental protocol on either a single slice
14 CT (Siemens Medical Solutions, Erlangen Germany) or a four slice detector CT (Toshiba Aquilon,
15 Toshiba Medical Systems, Zoetermeer, The Netherlands).

16 Pediatric effective doses for chest radiographs, abdominal films and barium studies were
17 calculated using the presets for pediatric patients aged 1, 5, 10 and 15 years in the software
18 package PCXMC (version 1.5)²⁵ in conjunction with local hospital exposure parameters and
19 protocols. Typified normalized effective doses for pediatric CT scanning were calculated based
20 on validated anatomically-specific Monte Carlo phantom simulations for 1, 5, 10 and 15 year
21 olds²³ (table 1).

1 Statistical Analysis:

2 The study period was divided into three tertiles of equal duration from 1st July 1992- 28th
3 February 1998 (Tertile 1), 1st March 1998-30th November 2003 (Tertile 2), and 1st December
4 2003-1st May 2009 (Tertile 3). Data compilation and statistical analyses were performed using
5 Microsoft Access 2007 (Microsoft Corporation, Washington, USA) and SPSS version 15 (SPSS Inc,
6 Chicago IL, USA). Algorithms calculating the age of each patient at time of scanning and
7 adjusting to the closest categorical age of 1, 5, 10, 15 years old or adult as appropriate were
8 established and the person years of follow up in each tertile determined. Comparison between
9 groups was performed using Mann Whitney U tests or Pearson's Chi-squared for categorical
10 variables. Spearman analysis was used for comparisons of non-parametric data where
11 appropriate. Comparison across 3 or more groups was performed using ANOVA or Kruskal
12 Wallis tests in accordance with their distribution. A type I error rate ≤ 0.05 was considered
13 significant.

14 Results:

15 Study population: 230 patients met inclusion criteria and were included in the final analysis.
16 The mean age of patients at the end of tertile 3 was 21.5 years (SD +/-11.6); mean FEV₁ %
17 predicted was 65.8% (SD +/- 27.3%). 7 patients received lung transplantations during the study
18 period and 42 patients died during the study period, 1 from hepatocellular carcinoma.

19 Imaging Modality:

1 There were 5596 radiological procedures: General radiographs n= 4730, Ultrasonography n=
2 406, CT n= 241, interventional procedures n=127, fluoroscopy n=74 and nuclear medicine n=18,
3 over the 2,240 person years of follow up.

4 Cumulative Effective Dose:

5 Over the total study period 1 patient (0.43%) had a CED >75mSv, 6 patients (2.6%) had a CED
6 50-75mSV, 30 patients (13%) had a CED 20-50mSv, 26 patients (11.3%) had a CED 10-20mSv, 29
7 patients (12.6%) had a CED 5-10mSV and 138 patients (60%) had a CED between 0-5mSv. In
8 total 63/230 (27.4%) of patients had a CED >10mSv over the study period. Plain radiographs
9 account for 74% of the total number of studies, resulting in 6% of total cumulative radiation
10 exposure for the most recent tertile (tertile 3, see figure 1). Conversely, CT accounted for 8% of
11 total number of studies whilst resulting in 74.8% of total radiation exposure in tertile 3 (Figure
12 1). A breakdown analysis of the 10% of patients with the highest CED showed 61.9% related to
13 CT, 10.4% from fluoroscopy, 12.7% from general radiography and 15.0% from interventional
14 procedures.

15

16 Changing trends over time:

17 The mean number of radiological procedures for tertile 1-3 was 2.89 procedures per person per
18 year for tertile 1, 2.7 procedures per person per year for tertile 2 and 2.71 procedures per
19 person per year for tertile 3. The equivalent annual mean effective dose (aMED) was 0.39 mSv
20 per person per year for tertile 1, 0.47mSv per person per year for tertile 2 and 1.67mSv per
21 person per year for tertile 3 ($p<0.001$) (table 2). The increased aMED predominantly related to

1 a 5.9 fold increase in the number of CT studies over this time ($p < 0.001$). Similar trends were
2 seen in the pediatrics' subgroup analysis (table 2).

3 Correlation between clinical phenotype and CED: CED correlated with age ($r = 0.307$; $p < 0.001$)
4 and in subgroup analysis of adult patients at the end of tertile 3, CED correlated inversely with
5 FEV₁% predicted ($r = 0.182$; $p < 0.04$). There was no correlation between mean annual effective
6 dose and gender ($p = 0.125$) or cystic fibrosis class mutation ($p = 0.122$).

7 **Anatomical Area Imaged:**

8 Cumulative radiation exposure, for the whole population, from thoracic imaging, as a
9 percentage of total CED was 46.9% over the 3 tertiles with relative exposure of 36%; 34.4% and
10 51.7% for tertiles 1-3 respectively, correlating with the increased use of CT thorax. Of the total
11 radiation exposure to the thorax, 76.4% (748mSv) was from CT thorax ($n = 130$ scans of thoracic
12 region), 9.5% (71.3mSv) from plain radiography, 0.8% (7.93mSv) from fluoroscopy, and 15.5%
13 (152mSv) from interventional procedures (figure 2)

14 Cumulative radiation exposure, for the whole population, from abdominal imaging as a
15 percentage of total CED was 42.7% over the 3 tertiles with cumulative exposure per tertile of
16 50%; 45.3% and 41% for tertiles 1-3 respectively reflecting both an increased use of abdomino-
17 pelvic CT imaging with a decreasing use in fluoroscopy. Overall the CED to the abdomino-pelvic
18 area increased significantly across the 3 tertiles, however there was a relative decrease in the
19 percentage contribution from abdomino-pelvic imaging due to the more significant increase in
20 thoracic imaging over the same time period. Of the total radiation exposure to the abdomino-

1 pelvic region; 53.5% was from abdomino-pelvic CT imaging, 11.9% from plain radiography,
2 25.6% from fluoroscopy, and 9.0% from interventional procedures.

3

4 **Discussion:**

5 This is the first study to calculate annual CED from all diagnostic imaging and interventional
6 radiology procedures in patients with cystic fibrosis. 27.3% of our patients had an estimated
7 CED exposure of >10mSv over the study period. Although controversial, an exposure of 10mSv
8 of radiation dose has been predicted to result on average in 1 radiation induced malignancy per
9 1000 patients¹⁰. Recent studies have highlighted the increased risk for certain malignancies in
10 patients with CF⁸. Several epidemiological studies have shown direct evidence of increased
11 cancer-related mortality following long-term exposure to low levels of ionizing radiation,
12 including diagnostic radiation^{10,26}, and that this cancer risk follows a “linear no threshold” risk,
13 indicating all radiation exposure may pose a risk of developing cancer²⁷. Studies have suggested
14 that the majority of physicians are not aware of the effective radiation dose associated with
15 radiological procedures, nor do they discuss the risks and benefits of CT and other imaging
16 examinations with their patients²⁸. One study found 75% of radiologists and physicians
17 significantly underestimated the radiation dose from a CT scan²⁸. Our paper address’s these
18 issues and generates a summary of effective doses for common adult and pediatric imaging
19 modalities, which clinicians can apply to their practice.

20 The present study demonstrates a significant increase in the annual mean effective dose to our
21 patients over the past 17 years, with a mean annual exposure of 1.67mSv per patient in the

1 most recent tertile. This dose may appear relatively modest, given for example a background
2 environmental radiation exposure annually of $\sim 3.9\text{mSv/yr}$ amongst the Irish population²⁹,
3 however this represents a significant exposure for such a young cohort of patients, made all the
4 more pertinent given the progressive increased life expectancy for these patients with
5 improved management of cystic fibrosis⁴. Over the 3 tertiles the frequency of medical imaging
6 remained relatively constant; however there was a significant shift in the use of imaging
7 modalities. The single largest contributing factor to the increased radiation exposure was the
8 5.9 fold increase in all CT imaging (thoracic, abdomino-pelvic and other) from the 1st tertile to
9 the 3rd tertile. This is consistent with international data on the rapidly increasing availability
10 and utilization of CT imaging in clinical medicine³⁰.

11 The changing trends in radiation exposure held similar results for both adult and pediatric
12 populations. The pediatric effective doses we established, are frequently much larger than
13 adult doses (table 1), this is due to the thinner torso in children providing less shielding of
14 organs from the radiation exposure¹. In CT, based on the exposure factors used and in the
15 absence of tube current modulation, there is a decrease in effective dose with increasing age.
16 This relates to the increased dose administered per unit of body mass for children as
17 highlighted recently in the “Image Wisely” campaign of the joint North American task force on
18 adult radiation protection³¹. Plain film radiography, however allows for greater dose reduction
19 in children, as the exposure parameters required are significantly lower than those used in CT.
20 Increased radiosensitivity in children still exists but the radiation dose decreases with
21 decreasing age, resulting overall in a decreasing effective dose³². The increasing use of CT
22 imaging as a routine procedure in some centers and the recent studies which suggest that HRCT

1 findings frequently pre-date changes in lung function and chest radiograph for pediatric
2 patients, highlights the need to develop further strategies to minimize the risks of radiation
3 exposure to these patients³³. Children, particularly females, are inherently more sensitive to
4 radiation exposure. This radiosensitivity relates to a large proportion of dividing cells and a
5 longer time for a potential cancer to develop¹. De Gonzalez et al estimated the lifetime risk of
6 radiation induced cancer for CF patients from a modern HRCT thorax protocol at 2 years of age
7 to be 24 per 100,000 for females versus 6 per 100,000 males, reducing to 1 per 100,000 for a 50
8 year old female and 0.3 per 100,000 for a 50 year old male³⁴. The studies to date predicting
9 radiation induced cancer risk from annual thoracic CT for CF patients³⁴ have assumed the
10 cancer rates to be the same as the general population, however recent data supports an
11 increased standardized incidence risk ratios for all cancers in CF patients, suggesting these
12 patients may have an intrinsic increased risk of malignancy. For anatomical reasons, the
13 thyroid radiation exposure is higher in pediatric patients undergoing chest radiographs and
14 thoracic CT imaging and the routine use of thyroid and breast shields should be seriously
15 considered in this cohort of patients³⁵.

16 Despite the fact that greater than 90% of CF patients die from respiratory failure, this study
17 highlights that over half of all radiation exposure is related to extra thoracic imaging modalities,
18 contrary to what one might have expected. CF is a multi-system disorder and patients with
19 cystic fibrosis are particular prone to both primary and secondary gastrointestinal disturbances
20 including constipation, distal intestinal obstruction syndrome, acute and chronic pancreatitis
21 and nutritional deficiency. These conditions frequently require diagnostic imaging, which is
22 often of a significantly higher³⁶ radiation dose than thoracic imaging³⁶. In our cohort of patients,

1 42.7% of radiological imaging was directed at the abdomino-pelvic region. There are consistent
2 reports of an increased standardized incidence ratio for digestive tract and other abdominal
3 malignancies in CF patients compared to the general population^{8,37}. This malignancy risk is
4 likely to be multifactorial, potentially as a result of the inflammation associated with chronic
5 pancreatitis³⁸, low serum vitamin D levels and an increasing frequency of lung transplantation
6 with associated immunosuppression³⁹. The high abdomino-pelvic radiation exposure is likely to
7 pose an additional risk factor for these malignancies.

8 There are a number of available strategies for reducing radiation exposure in patients with CF⁴⁰.
9 Patients with CF frequently have a smaller body habitus and reduced body mass indices, so
10 specific low-dose CF protocols optimizing specific parameters such as the millamperes (mA) to
11 patient weight need to be considered⁴¹. Reducing the mAs from 180 to 45 for a conventional
12 thoracic HRCT scan can result in a 4 fold reduction in radiation exposure without any significant
13 difference in image quality⁴². Additionally, over 97% of CT Thorax scans have significant supra-
14 apical and infra-pulmonary unnecessary imaging, resulting in increased exposures to the
15 thyroid and abdominal regions⁴³. For incremental CT thorax imaging in CF patients, the validity
16 of reducing the number of images per CT examination has generated conflicting results, one
17 study has shown an equivalent score using CT cuts from 6 pre-selected sections in a cohort of
18 children with CF⁴⁴, whilst others report a reduced sensitivity to detect changes when the image
19 interval is >10mm in children with CF⁴⁵. With proper attention to detail of scanning
20 parameters radiation dose can be reduced substantially compared to routine chest CT.
21 Strategies currently available for optimization of CT radiation dose include the use of automatic
22 tube current modulation, iterative reconstruction techniques and noise reduction filters which

1 can lead to significant reduction in radiation exposure without significant impact on image
2 quality²⁷. As a result of the preliminary results of this study, we recently implemented a new
3 thoracic low dose thin slice CT protocol for pediatric patients with CF which achieved significant
4 reductions in mean effective doses¹⁴. Close attention needs to be given to the information
5 gained from each imaging request to ensure that the examination is indicated and could not be
6 replaced by an imaging study which does not expose the patient to ionizing radiation (e.g.
7 ultrasound or MRI). Also it is very important to limit exposure to extra-thoracic organs
8 including the development of low dose abdomino-pelvic CT protocols.

9 The advantage of detecting early changes on CT imaging awaits additional confirmation, some
10 authorities feel strongly that the structural information gained by the use of CT scanning helps
11 to tailor treatments, reducing under and over treatment for patients, but to date there are no
12 studies proving such a benefit^{13 19}. The current guidelines suggest there is insufficient evidence
13 to recommend use of chest CT scans for routine surveillance but suggest chest CT scanning may
14 be helpful in infants with symptoms or signs of lung disease who fail to respond to basic
15 interventions⁴⁶. Future studies are also needed to delineate the role of novel strategies in
16 thoracic imaging, including the use of hyperpolarized helium magnetic resonance imaging⁴⁷
17 and positron emission tomography⁴⁰.

18 This study has a number of limitations, notably it represents the radiation exposure in a
19 single tertiary referral cystic fibrosis center. However, the use of a nationally designated CF
20 center acting as both the primary and secondary care facility, regardless of health insurance
21 status, ensured the accuracy of capturing of all imaging studies for this cohort of patients. We

1 acknowledge that retrospective radiation dose exposures appropriate for the period of study
2 involved were used. With technological advances it has been suggested that a reduction in
3 radiation exposure of over 75% can be safely achieved using more modern low-dose CT thorax
4 protocols⁴⁸, however this may be offset with the increasing use of spiral CT scanning and
5 potentially by the recent suggestions to monitor disease progression using combined PET/CT
6 imaging⁴⁹⁻⁵⁰. The modern use of helical CT scanning in CF patients⁵¹ has increased the diagnostic
7 sensitivity in detecting peripheral thoracic changes³³ but incurs significantly higher radiation
8 exposures compared to standard incremental scans of up to 3 mSv per CT thorax. Inevitably
9 there will be variation in clinical practice between centers', one previous French study
10 identified a mean cumulative effective dose from CT scans in CF patients of 19.5 mSv⁵², with a
11 mean patient exposure to 3.4 CT scans. The annual radiation exposure in our cohort of patients
12 with CF is relatively low, with mean annual exposures of 1.667mSv in the most recent tertile 3,
13 this compares to an annual exposure dose of 8.1mSv in a cohort of patient with Crohn's disease
14 at the same institute. It is important to note that only 1 patient (0.43%) had an exposure of
15 >75mSv over the 17 yr period, compared to 15.5% of Crohn's patients¹⁵ and 13% of
16 hemodialysis patients having an exposure of >75mSv over the same time period at our
17 institute¹⁶. However, the critical difference is the young age patients with CF are exposed to
18 radiation and the chronic progressive nature of CF from early childhood. Our center follows the
19 3 fundamental principles of radiation protection: justification, dose optimization through the
20 "as low as reasonably achievable" (ALARA) principle and dose limitation, as set out in the
21 International Commission of Radiological Protection⁵³. As a result of this, we have not yet
22 adopted the use of routine CT scanning into clinical practice given the absence of any proven

1 benefit in clinical outcome for such a measure⁵². This study is therefore likely to represent a
2 conservative estimate for the annual cumulative effective dose for radiological imaging in CF
3 patients and for the changing trends in CT imaging over the past 17 years. Urgent consideration
4 should be given to the development of low-dose imaging protocols and to regular monitoring
5 and recording of CED for patients, particularly in identifiable groups where exposure levels may
6 become high, as in our cohort and in many chronic diseases. Strategies to prospectively
7 monitor cumulative dose may include recommendations such as: the creation of dose
8 registries; the mandatory recording of dose within the examination images or report, recording
9 of dose within the patient's medical record and mandatory accreditation of imaging facilities.
10 As a result of this study we are currently implementing a policy of recording the effective dose
11 through the picture archive communication system (PACS) at our institute, to allow for ongoing
12 monitoring and auditing of radiation exposure with each imaging examination⁵⁴.

13 **Conclusion:**

14 Patients with CF are exposed to high radiation doses from a young age, exacerbated by the
15 increasing use in CT imaging. Strategies need to be developed and implemented with regard to
16 radiation exposure reduction for both thoracic and extra-thoracic imaging in this cohort of
17 patients.

18 **Disclosures:**

19 There are no competing interests for this paper. The authors grant exclusive publishing rights
20 to the journal, and full ethics board approval was obtained as outlined in the body of the paper.

21 **References:**

22

- 1 1. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. *N Engl J Med*
2 2007;357(22):2277-84.
- 3 2. de Jong PA, Mayo JR, Golmohammadi K, Nakano Y, Lequin MH, Tiddens HA, et al. Estimation of cancer
4 mortality associated with repetitive computed tomography scanning. *Am J Respir Crit Care Med*
5 2006;173(2):199-203.
- 6 3. Preston DL, Shimizu Y, Pierce DA, Suyama A, Mabuchi K. Studies of mortality of atomic bomb
7 survivors. Report 13: Solid cancer and noncancer disease mortality: 1950-1997. *Radiat Res*
8 2003;160(4):381-407.
- 9 4. Pierce DA, Preston DL. Radiation-related cancer risks at low doses among atomic bomb survivors.
10 *Radiat Res* 2000;154(2):178-86.
- 11 5. Bush A. Treatment of cystic fibrosis: time for a new paradigm? *Chest* 2009;136(5):1197-9.
- 12 6. Jones AM, Dodd ME, Morris J, Doherty C, Govan JR, Webb AK. Clinical outcome for cystic fibrosis
13 patients infected with transmissible pseudomonas aeruginosa: an 8-year prospective study.
14 *Chest*;137(6):1405-9.
- 15 7. Dodge JA, Lewis PA, Stanton M, Wilsher J. Cystic fibrosis mortality and survival in the UK: 1947-2003.
16 *Eur Respir J* 2007;29(3):522-6.
- 17 8. Johannesson M, Askling J, Montgomery SM, Ekblom A, Bahmanyar S. Cancer risk among patients with
18 cystic fibrosis and their first-degree relatives. *Int J Cancer* 2009;125(12):2953-6.
- 19 9. Pierce DA, Shimizu Y, Preston DL, Vaeth M, Mabuchi K. Studies of the mortality of atomic bomb
20 survivors. Report 12, Part I. Cancer: 1950-1990. *Radiat Res* 1996;146(1):1-27.
- 21 10. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation NRC. *Health*
22 *Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2*. Washington, DC: The
23 National Academies Press, 2006.
- 24 11. Desmond AN, O'Regan K, Curran C, McWilliams S, Fitzgerald T, Maher MM, et al. Crohn's disease:
25 factors associated with exposure to high levels of diagnostic radiation. *Gut* 2008;57(11):1524-29.
- 26 12. Aziz ZA, Davies JC, Alton EW, Wells AU, Geddes DM, Hansell DM. Computed tomography and cystic
27 fibrosis: promises and problems. *Thorax* 2007;62(2):181-86.
- 28 13. Santamaria F, Grillo G, Guidi G, Rotondo A, Raia V, de Ritis G, et al. Cystic fibrosis: when should high-
29 resolution computed tomography of the chest be obtained? *Pediatrics* 1998;101(5):908-13.
- 30 14. O'Connor OJ, Vandeleur M, McGarrigle AM, Moore N, McWilliams SR, McSweeney SE, et al.
31 Development of low-dose protocols for thin-section CT assessment of cystic fibrosis in pediatric
32 patients. *Radiology* 2010;257(3):820-9.
- 33 15. Judge EP, Dodd JD, Masterson JB, Gallagher CG. Pulmonary abnormalities on high-resolution CT
34 demonstrate more rapid decline than FEV1 in adults with cystic fibrosis. *Chest*
35 2006;130(5):1424-32.
- 36 16. Vilozni D, Bentur L, Efrati O, Minuskin T, Barak A, Szeinberg A, et al. Spirometry in early childhood in
37 cystic fibrosis patients. *Chest* 2007;131(2):356-61.
- 38 17. Robinson TE, Goris ML, Zhu HJ, Chen X, Bhise P, Sheikh F, et al. Dornase alfa reduces air trapping in
39 children with mild cystic fibrosis lung disease: a quantitative analysis. *Chest* 2005;128(4):2327-
40 35.
- 41 18. Tiddens HA, de Jong PA. Imaging and clinical trials in cystic fibrosis. *Proc Am Thorac Soc*
42 2007;4(4):343-6.
- 43 19. de Jong PA, Lindblad A, Rubin L, Hop WC, de Jongste JC, Brink M, et al. Progression of lung disease on
44 computed tomography and pulmonary function tests in children and adults with cystic fibrosis.
45 *Thorax* 2006;61(1):80-5.
- 46 20. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced
47 ventilatory flows. Report Working Party Standardization of Lung Function Tests, European

- 1 Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur*
 2 *Respir J Suppl* 1993;16:5-40.
- 3 21. Radiation protection in medicine. ICRP Publication 105. *Ann ICRP* 2007;37(6):1-63.
- 4 22. Kinsella SM, Coyle JP, Long EB, McWilliams SR, Maher MM, Clarkson MR, et al. Maintenance
 5 hemodialysis patients have high cumulative radiation exposure. *Kidney Int* 2010;78(8):789-93.
- 6 23. Mettler FA, Jr., Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic
 7 nuclear medicine: a catalog. *Radiology* 2008;248(1):254-63.
- 8 24. Hart D, Wall B. Radiation exposure of the UK population from medical and dental X-ray
 9 examinations: National Radiation Protection Board, 2002.
- 10 25. Tapiovaara M, Lakkisto M, Servomaa A. PCXMC- a PC based Monte Carlo program for calculating
 11 patient doses in medical x-ray examinations. Helsinki: Finnish Centre for radiation and nuclear
 12 Safety (STUK), 1997:1-46.
- 13 26. Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, et al. The 15-Country Collaborative
 14 Study of Cancer Risk among Radiation Workers in the Nuclear Industry: estimates of radiation-
 15 related cancer risks. *Radiat Res* 2007;167(4):396-416.
- 16 27. Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, et al. Cancer risks attributable to low
 17 doses of ionizing radiation: assessing what we really know. *Proc Natl Acad Sci U S A*
 18 2003;100(24):13761-6.
- 19 28. Lee CI, Haims AH, Monico EP, Brink JA, Forman HP. Diagnostic CT scans: assessment of patient,
 20 physician, and radiologist awareness of radiation dose and possible risks. *Radiology*
 21 2004;231(2):393-8.
- 22 29. Colgan PA OC, Hone C, Fenton D. Radiation Doses Received by the Irish Population.
 23 [http://www.rpii.ie/getdoc/003644df-6cf8-428f-9752-ba24af66bf09/Radiation-Doses-](http://www.rpii.ie/getdoc/003644df-6cf8-428f-9752-ba24af66bf09/Radiation-Doses-Received.aspx)
 24 [Received.aspx](http://www.rpii.ie/getdoc/003644df-6cf8-428f-9752-ba24af66bf09/Radiation-Doses-Received.aspx) 2008.
- 25 30. Kalra MK, Maher MM, Toth TL, Hamberg LM, Blake MA, Shepard JA, et al. Strategies for CT radiation
 26 dose optimization. *Radiology* 2004;230(3):619-28.
- 27 31. Brink JA, Amis ES. Image Wisely: A Campaign to Increase Awareness about Adult Radiation
 28 Protection. *Radiology* 2010;257(3):601-02.
- 29 32. Hintenlang K, Williams J, Hintenlang D. A survey of radiation dose associated with pediatric plain-film
 30 chest X-ray examinations. *Pediatric Radiology* 2002;32(11):771-77.
- 31 33. Dodd JD, Souza CA, Muller NL. Conventional high-resolution CT versus helical high-resolution MDCT
 32 in the detection of bronchiectasis. *AJR Am J Roentgenol* 2006;187(2):414-20.
- 33 34. de Gonzalez AB, Kim KP, Samet JM. Radiation-induced cancer risk from annual computed
 34 tomography for patients with cystic fibrosis. *Am J Respir Crit Care Med* 2007;176(10):970-3.
- 35 35. Hopper KD, King SH, Lobell ME, TenHave TR, Weaver JS. The breast: in-plane x-ray protection during
 36 diagnostic thoracic CT--shielding with bismuth radioprotective garments. *Radiology*
 37 1997;205(3):853-8.
- 38 36. Littlewood JM. Gastrointestinal complications in cystic fibrosis. *J R Soc Med* 1992;85 Suppl 19:13-9.
- 39 37. Neglia JP, FitzSimmons SC, Maisonneuve P, Schoni MH, Schoni-Affolter F, Corey M, et al. The risk of
 40 cancer among patients with cystic fibrosis. Cystic Fibrosis and Cancer Study Group. *N Engl J Med*
 41 1995;332(8):494-9.
- 42 38. Demaria S, Pikarsky E, Karin M, Coussens LM, Chen YC, El-Omar EM, et al. Cancer and inflammation:
 43 promise for biologic therapy. *J Immunother*;33(4):335-51.
- 44 39. Cohen AH, Sweet SC, Mendeloff E, Mallory GB, Jr., Huddleston CB, Kraus M, et al. High incidence of
 45 posttransplant lymphoproliferative disease in pediatric patients with cystic fibrosis. *Am J Respir*
 46 *Crit Care Med* 2000;161(4 Pt 1):1252-5.
- 47 40. de Jong PA, Tiddens HA, Lequin MH, Robinson TE, Brody AS. Estimation of the radiation dose from CT
 48 in cystic fibrosis. *Chest* 2008;133(5):1289-91; author reply 90-1.

- 1 41. Long FR. High-resolution computed tomography of the lung in children with cystic fibrosis: technical
2 factors. *Proc Am Thorac Soc* 2007;4(4):306-9.
- 3 42. Lucaya J, Piqueras J, Garcia-Pena P, Enriquez G, Garcia-Macias M, Sotil J. Low-dose high-resolution CT
4 of the chest in children and young adults: dose, cooperation, artifact incidence, and image
5 quality. *AJR Am J Roentgenol* 2000;175(4):985-92.
- 6 43. Campbell J, Kalra MK, Rizzo S, Maher MM, Shepard JA. Scanning beyond anatomic limits of the
7 thorax in chest CT: findings, radiation dose, and automatic tube current modulation. *AJR Am J*
8 *Roentgenol* 2005;185(6):1525-30.
- 9 44. Jimenez S, Jimenez JR, Crespo M, Santamarta E, Bousoño C, Rodriguez J. Computed tomography in
10 children with cystic fibrosis: a new way to reduce radiation dose. *Arch Dis Child* 2006;91(5):388-
11 90.
- 12 45. de Jong PA, Nakano Y, Lequin MH, Tiddens HA. Dose reduction for CT in children with cystic fibrosis:
13 is it feasible to reduce the number of images per scan? *Pediatr Radiol* 2006;36(1):50-3.
- 14 46. Borowitz D, Robinson KA, Rosenfeld M, Davis SD, Sabadosa KA, Spear SL, et al. Cystic Fibrosis
15 Foundation Evidence-Based Guidelines for Management of Infants with Cystic Fibrosis. *The*
16 *Journal of Pediatrics* 2009;155(6, Supplement 1):S73-S93.
- 17 47. Altes TA, Eichinger M, Puderbach M. Magnetic resonance imaging of the lung in cystic fibrosis. *Proc*
18 *Am Thorac Soc* 2007;4(4):321-7.
- 19 48. Huda W. Radiation doses and risks in chest computed tomography examinations. *Proc Am Thorac*
20 *Soc* 2007;4(4):316-20.
- 21 49. Klein M, Cohen-Cyberknoh M, Armoni S, Shoseyov D, Chisin R, Orevi M, et al. 18F-
22 fluorodeoxyglucose-PET/CT imaging of lungs in patients with cystic fibrosis. *Chest*
23 2009;136(5):1220-8.
- 24 50. Dolovich MB, Schuster DP. Positron emission tomography and computed tomography versus
25 positron emission tomography computed tomography: tools for imaging the lung. *Proc Am*
26 *Thorac Soc* 2007;4(4):328-33.
- 27 51. Davis SD, Brody AS, Emond MJ, Brumback LC, Rosenfeld M. Endpoints for clinical trials in young
28 children with cystic fibrosis. *Proc Am Thorac Soc* 2007;4(4):418-30.
- 29 52. Donadieu J, Roudier C, Saguintaah M, Maccia C, Chiron R. Estimation of the radiation dose from
30 thoracic CT scans in a cystic fibrosis population. *Chest* 2007;132(4):1233-8.
- 31 53. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP
32 publication 103. *Ann ICRP* 2007;37(2-4):1-332.
- 33 54. AlSuwaidi JS, Bayoumi M, Al Shibli N, Sulaiman H, URrahman T, Al Yarah M. Utilisation of PACS to
34 monitor patient CT doses. *Radiation Protection Dosimetry* 2011.
- 35
36

37 **Legend for Table 1: The effective doses of frequent medical imaging procedures used for CF**
38 **patients.**

39

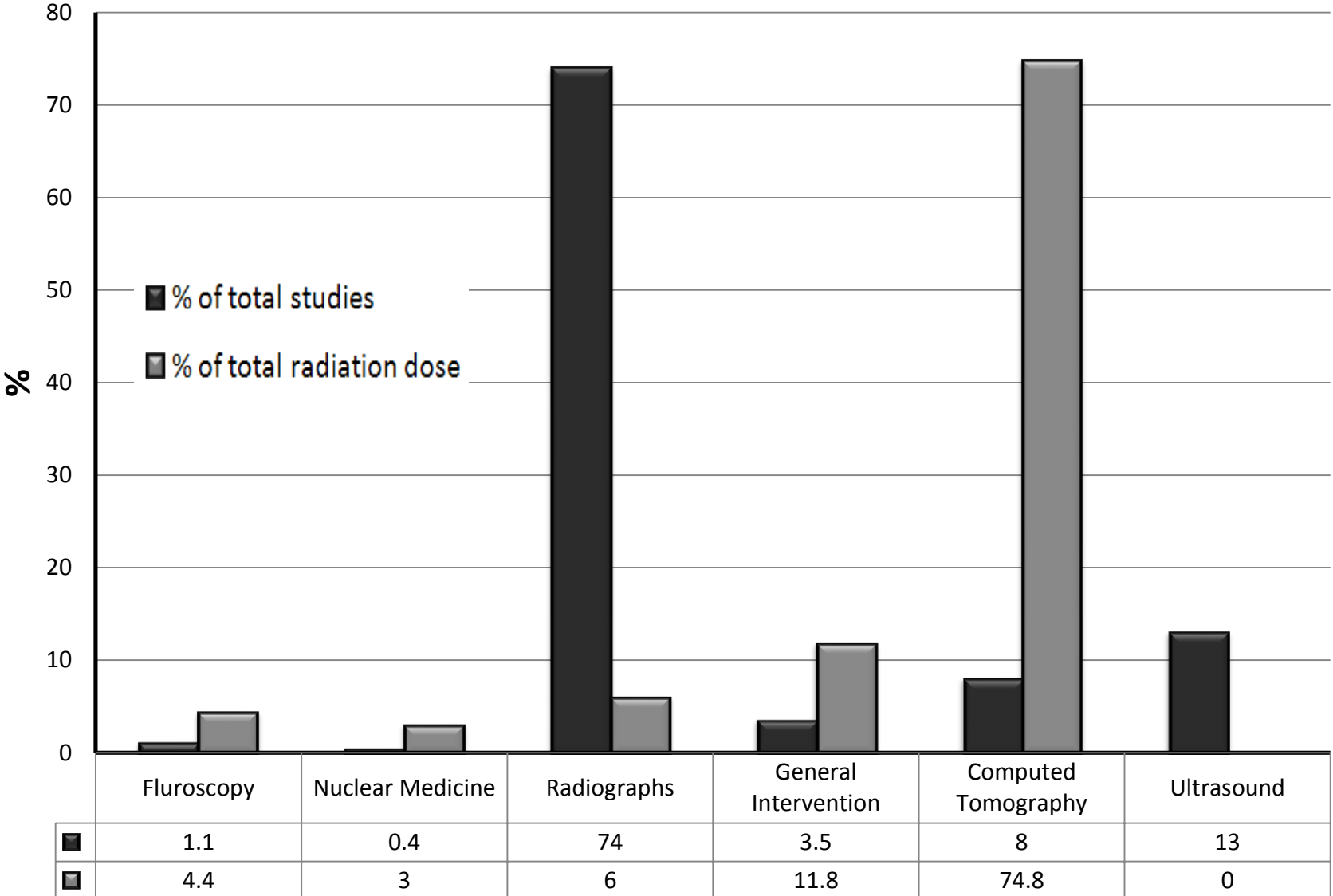
40 **Legend for Table 2: Total radiation dose per patient year (PPY) across the 3 tertiles for all**
41 **study subjects and secondly for pediatric patients only.**

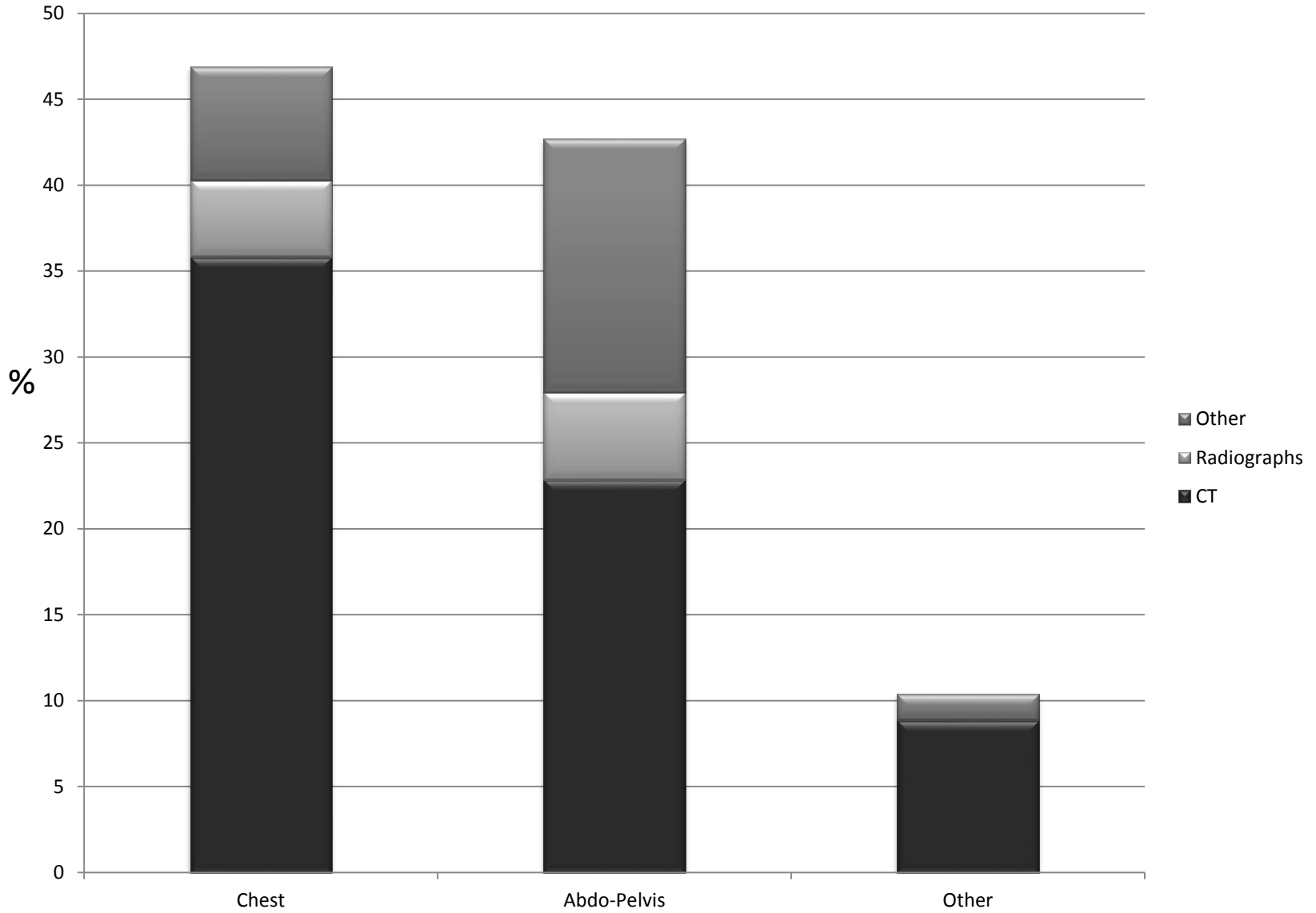
- 1 **Legend for Figure 1: Relative contribution of each radiological imaging modality to cumulative**
- 2 **radiation exposure for tertile 3.**

- 3 **Legend for Figure 2: Regional percentage breakdown of total radiation dose exposure to**
- 4 **thorax, abdomino-pelvic and other body parts over tertiles 1-3 for the studied population**
- 5 **(adult and pediatric inclusive).**

Procedure	1yr (mSv)	5yr (mSv)	10yr (mSv)	15yr (mSv)	≥18yr (mSv)
CXR PA	0.003	0.005	0.01	0.014	0.02
Radiograph of abdomen	0.02	0.04	0.1	0.14	0.23
Conventional CT Thorax	13.3	11.2	9.8	7.7	7.0
HRCT Thorax	2.85	2.4	2.1	1.65	1.5
CT abdomen	16	12.8	12	8.8	8
CT Pulmonary Angiogram	28.5	24	21	18	15
Barium Meal	1.28	0.82	0.93	1.63	2.32
Barium Swallow	1.16	0.78	1.09	0.75	0.77
Radiograph Lumbar Spine					1.5

Population	All subjects				Pediatrics only			
	1st	2nd	3rd	p-value	1st	2nd	3rd	p-value
Tertile								
Number of subjects	132	157	199		105	115	115	
Cumulative Follow Up (years)	599.8	702.6	938.0		435.83	452.17	470.67	
All investigations								
Number PPY	2.89	2.70	2.71	0.86	2.82	2.49	2.04	0.11
Total dose PPY, (mSv)	0.39	0.47	1.667	<0.001	0.403	0.303	0.788	0.01
Chest Radiographs only								
No. PPY	2.07	1.93	1.66	0.31	1.98	1.76	1.35	0.03
Total dose PPY, (mSv)	0.03	0.03	0.03	0.92	0.02	0.02	0.02	0.22
Abdominal Radiographs Only								
No. PPY	0.23	0.24	0.19	0.81	0.23	0.27	0.07	0.11
Total dose PPY, (mSv)	0.03	0.03	0.04	0.76	0.03	0.03	0.008	0.07
Total CT								
No. PPY	0.035	0.046	0.210	<0.001	0.042	0.033	0.108	0.006
Total dose PPY (mSv)	0.136	0.179	1.27	<0.001	0.192	0.084	0.581	0.002
Thoracic CTs only								
No. PPY	0.015	0.018	0.125	<0.001	0.024	0.018	0.063	0.01
Total dose PPY, (mSv)	0.087	0.061	0.778	<0.001	0.146	0.045	0.327	0.02
Abdomino-Pelvic CT Only								
No. of PPY	0.001	0.010	0.058	<0.001	0.002	0.002	0.028	0.001
Total dose PPY, (mSv)	0.008	0.082	0.444	<0.001	0.010	0.012	0.218	0.001
Other CTs								
No. PPY	0.019	0.018	0.027	0.65	0.017	0.014	0.018	0.94
Total dose PPY (mSv)	0.041	0.036	0.054	0.68	0.036	0.027	0.036	0.92
Total interventional studies								
No. of PPY	0.034	0.039	0.101	0.01	0.018	0.016	0.033	0.55
Total dose PPY (mSv)	0.038	0.069	0.172	0.06	0.019	0.008	0.086	0.06
Total Barium Studies								
No. PPY	0.048	0.039	0.014	0.01	0.048	0.048	0.012	0.03
Total dose PPY (mSv)	0.104	0.093	0.055	0.36	0.096	0.107	0.026	0.05
Total Nuclear Medicine Studies								
No. PPY	0.001	0.009	0.011	0.29	0.002	0.008	0.006	0.37
Total dose PPY (mSv)	0.009	0.051	0.063	0.37	0.011	0.038	0.034	0.49





Radiological imaging in cystic fibrosis: cumulative effective dose & changing trends over 2 decades

O. J. O'Connell, S. McWilliams, A. M. McGarrigle, O. J. O'Connor, F. Shanahan, D. Mullane, J. Eustace, M. M. Maher and B. J. Plant
Chest; Prepublished online December 29, 2011;
DOI 10.1378/chest.11-1972

This information is current as of January 19, 2012

Updated Information & Services

Updated Information and services can be found at:

<http://chestjournal.chestpubs.org/content/early/2011/12/28/chest.11-1972>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Reprints

Information about ordering reprints can be found online:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Citation Alerts

Receive free e-mail alerts when new articles cite this article. To sign up, select the "Services" link to the right of the online article.

Images in PowerPoint format

Figures that appear in *CHEST* articles can be downloaded for teaching purposes in PowerPoint slide format. See any online figure for directions.

CHEST Papers in Press are peer-reviewed, accepted articles that have not yet been published in an issue of the journal and have not yet been edited or typeset. The final version may contain substantive or nonsubstantive changes. These articles are indexed by PubMed, but any references to an in-press article must include the digital object identifier (DOI) and date of in-press publication.

CHEST Papers in Press are not under media or public embargo once they appear online. For inquiries, please contact the AACP Media Relations Department at (847) 498-1400 or media@chestnet.org.

