



# Optical imaging versus CT and plain radiography to quantify pectus severity: a systematic review and meta-analysis

Jean H. T. Daemen<sup>1</sup>, Tom G. J. Loonen<sup>2</sup>, Pieter W. J. Lozekoot<sup>1</sup>, Jos G. Maessen<sup>3,4</sup>, Thomas J. J. Maal<sup>2</sup>, Karel W. E. Hulsewé<sup>1</sup>, Yvonne L. J. Vissers<sup>1</sup>, Erik R. de Loos<sup>1</sup>

<sup>1</sup>Department of Surgery, Division of General Thoracic Surgery, Zuyderland Medical Centre, Heerlen, the Netherlands; <sup>2</sup>3D Lab Radboudumc, Radboud University Medical Centre, Nijmegen, the Netherlands; <sup>3</sup>Department of Cardiothoracic Surgery, Maastricht University Medical Centre, Maastricht, the Netherlands; <sup>4</sup>Faculty of Health, Medicine and Life Sciences (FHML), Cardiovascular Research Institute Maastricht (CARIM), Maastricht, the Netherlands

**Contributions:** (I) Conception and design: All authors; (II) Administrative support: TGJ Loonen, PWJ Lozekoot; (III) Provision of study materials or patients: JHT Daemen, TGJ Loonen, PWJ Lozekoot, ER de Loos; (IV) Collection and assembly of data: JHT Daemen, TGJ Loonen, ER de Loos; (V) Data analysis and interpretation: JHT Daemen, TGJ Loonen, TJJ Maal, KWE Hulsewé, YLJ Vissers, JG Maessen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

**Correspondence to:** Erik R. de Loos. Department of Surgery, Division of General Thoracic Surgery, Zuyderland Medical Centre, Henri Dunantstraat 5, 6419PC Heerlen, the Netherlands. Email: e.delooos@zuyderland.nl.

**Background:** Computed tomography (CT) and two-view chest radiographies are the most commonly used imaging techniques to quantify the severity of pectus excavatum (PE) and pectus carinatum (PC). Both modalities expose patients to ionizing radiation that should ideally be avoided, especially in pediatric patients. In an effort to diminish this exposure, three-dimensional (3D) optical surface imaging has recently been proposed as an alternative method. To assess its clinical value as a tool to determine pectus severity we conducted a systematic review in which we assessed all studies that compared 3D scan-based pectus severity measurements with those derived from CT-scans and radiographies.

**Methods:** Six scientific databases and three registries were searched through April 30th, 2019. Data regarding the correlation between severity measures was extracted and submitted to meta-analysis using the random-effects model and  $I^2$ -test for heterogeneity.

**Results:** Five observational studies were included, enrolling 75 participants in total. Pooled analysis of participants with PE demonstrated a high positive correlation coefficient of 0.89 [95% confidence interval (CI): 0.81 to 0.93;  $P < 0.001$ ] between the CT-derived Haller index (HI) and its 3D scan equivalent based on external measures. No heterogeneity was detected ( $I^2 = 0.00\%$ ;  $P = 0.834$ ).

**Conclusions:** 3D optical surface scanning is an attractive and promising imaging technique to determine the severity of PE without exposure to ionizing radiation. However, further research is needed to determine novel cut-off values for 3D scans to facilitate clinical decision making and help determine surgical candidacy. No evidence was found that supports nor discards the use of 3D scans to determine PC severity.

**Keywords:** Three-dimensional optical surface imaging (3D optical surface imaging); external Haller index (EHI); pectus excavatum (PE); pectus carinatum (PC)

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## Introduction

Pectus excavatum (PE) and pectus carinatum (PC) are the most common congenital chest wall deformities. The

latter is characterized by an outward protrusion of the sternum, while PE is characterized by an inward depression. PE occurs in 1:400 of live births (1), in comparison to PC

which is reported to occur 2–4 times less frequent (2). PE and PC may be associated with impaired body image perception and result in lowered self-esteem, psychological stress and diminished quality of life. Next to these psychological effects, PE may be associated with impaired cardiopulmonary function (3,4). The current gold standard to evaluate the extent of pectus deformities is computed tomography (CT). In patients with PE, CT is generally used to calculate the Haller index (HI) (5). The resulting HI is subsequently used in the process of decision making to determine surgical candidacy. In PC no such standard metric exists. Despite CT being the current gold standard, it inescapably implies exposure to ionizing radiation. Two-view chest radiographies may be used alternatively to CT, resulting in dose reduction. However, according to the doctrine of radiation hygiene, every effort should be made to avoid, or if not possible, limit radiation exposure, especially in pediatric patients with a long lifetime risk to develop radiation related pathologies (6,7). In an effort to diminish radiation exposure, alternative methods are being explored to quantify the extent of chest wall deformities, among which three-dimensional (3D) optical surface imaging shows great potential (8). This technology has been widely used to map the chest surface in scoliosis patients and may serve as a safe and non-invasive severity measurement tool that utilizes non-ionizing light illumination. Optical imaging produced trunk topographies have already been demonstrated to be clinically feasible and accurate (9,10). However, as stressed by Sarwar and colleagues (8), the exact clinical value (e.g., in the process of decision making, follow-up, et cetera) of this novel severity measurement technique in PE and PC is yet to be investigated. Consequently, the following research question was formulated: can the evaluation of pectus excavatum and carinatum severity through chest CTs and radiographies be replaced by 3D optical scans? To answer this question, we conducted a systematic review and pooled analysis of the currently available literature in which we assessed all studies that compared 3D optical scan-based severity measurements with those derived from CT-scans or chest radiographies in patients with PE and PC. To our knowledge no such comprehensive review has been conducted to date.

## Methods

### *Protocol and registration*

Prior to start, the review protocol was registered to the

PROSPERO registry (Record ID: CRD42019122860). In addition, this review was written in compliance with the PRISMA statements to ensure quality and transparency throughout (11).

### *Eligibility criteria*

#### **Types of participants**

Patients of any race, gender and age with PE or PC were considered for inclusion.

#### **Types of intervention**

Papers that performed pectus severity quantification based on 3D optical imaging and compared its performance to severity measurements based on chest radiographies or CT-scans were examined for eligibility. All optical surface imaging techniques, such as laser and structured (white) light, were considered for inclusion. Contact 3D scanners that probe the subject through physical touch were not considered.

#### **Primary outcome measure(s)**

Comparison of pectus severity measurements based on 3D optical surface scanning and the study's comparative measurement method (i.e., CT-scans or chest radiographies).

#### **Types of studies**

All observational and randomized studies adhering to the aforementioned criteria were assessed for eligibility. Studies reporting combined data on PE and PC severity measurements were considered only if data were presented separately.

### *Search and study selection*

Potentially eligible papers were identified by searching electronic scientific databases and trial registries. Solely articles reported in English were considered. No publication date restrictions were imposed. The search strategy was first applied to the PubMed database and subsequently adapted for EMBASE, Web of Science, the Cochrane Library, and CINAHL. In addition, the PROSPERO, WHO-ICTRP, and Clinicaltrials.gov registries were searched. See *Figures S1–S5* for the complete scientific database search queries. Identical queries were used to search the aforementioned registries. An additional manual cross-reference and related-articles search was conducted to identify articles that were not found through the prior search. This additional

step also functioned as an indicator of the quality and integrity of the database search strategy. All searches were performed by a certified librarian. The last search was run on April 30<sup>th</sup>, 2019. Articles resulting from the searches were judged for eligibility based on their title and abstract. Thereafter, full text of potentially eligible articles was read and assessed according to the predefined eligibility criteria. Papers meeting these criteria were included for systematic review, and if applicable, meta-analysis. Article selection was performed in a standardized, unblinded manner by two independent reviewers (Jean H. T. Daemen & Tom G. J. Loonen). Inter-reviewer disagreements were resolved by consultation of Erik R. de Loos.

### *Data collection and data items*

Data was extracted by one independent reviewer (Jean H. T. Daemen) and validated by a second reviewer (Tom G. J. Loonen). Inter-reviewer disagreements were resolved by consultation of Erik R. de Loos. To structure data extraction and presentation, an extraction sheet was developed and pilot-tested on two randomly selected included studies. The sheet was adopted accordingly. Data was extracted from each included paper on: (I) general study characteristics: study design, country and enrolment period; (II) characteristics of participants: number of included participants, gender, age, and the thoracic wall deformity that was studied (i.e., PE or PC); (III) characteristics of the optical scan(ner): scanner brand/type, scanning method, static or handheld, accuracy, acquisition and/or processing time, used software, patient position, and pectus severity measurement method; (IV) characteristics of the comparison: comparative technique (e.g., CT-scans or radiographies), and severity measurement method; (V) primary outcome measure: comparison of 3D optical surface scan- and radiography- or CT-based severity measurements. Continuous variables were denoted as mean, standard deviation (SD) and range. Continuous variables reported as median and interquartile range or standard error were converted. The primary outcome measure was extracted as reported. For studies that solely reported raw severity measurement data, Pearson's correlation coefficients ( $r$ ) were calculated using SPSS statistics (IBM Corp. Released 2017. IBM SPSS statistics for MacOS, version 25.0, Armonk, NY, USA). The Pearson's correlation coefficient was chosen as this was the most used metric to compare severity indices as found during the preliminary search. Missing P values were, if possible, calculated from the available data.  $P \leq 0.05$  was considered to

be statistically significant. To interpret the size of reported correlation coefficients, we used cut-off values as described by Mukaka (12). Correlation sizes that ranged from 0 to 0.30 were judged to be negligible, while correlations that ranged from 0.30 to 0.50, 0.50 to 0.70, 0.70 to 0.90, and 0.90 to 1.00 were interpreted as either low, moderate, high and very high.

### *Risk of bias in individual studies*

No validated tools exist that assess quality of correlation studies. Therefore, a tool was constructed (See *Figure 1*). This tool was adapted from the National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (13) and pilot tested on two randomly selected included studies. The tool was adopted accordingly. Questions were answered by Yes, No, not applicable (NA), or not reported (NR). Studies were, subsequently, given an overall quality judgement (Good, Fair, or Poor). This judgement was not based on simple summation of answers but based on the ability of studies to draw associative conclusions about the effect of the imaging techniques being studied on outcomes. Quality assessment was performed by two reviewers (Jean H. T. Daemen & Tom G. J. Loonen). Inter-reviewer disagreements were resolved by consultation of Erik R. de Loos.

### *Summary measures and synthesis of results*

Quantitative synthesis of the primary outcome measure was only performed if studies were sufficiently homogeneous, otherwise, data was reported as such. For quantitative synthesis, correlation coefficients were converted into Z-scores using the Fisher Z-transformation method. Resulting Z-scores were pooled using the random-effects model. Pooled Z-scores and their corresponding 95% confidence interval (95% CI) were converted back into pooled correlation coefficients to allow easy interpretation. No additional analyses were performed. The  $I^2$ -test for statistical heterogeneity was used as a measure of consistency.  $I^2$  values greater than 50%, with a P value  $\leq 0.10$  indicated the presence of substantial heterogeneity. Meta-analyses were performed by ProMeta 3.0 software for MacOS (based on ProMeta 2.1, deployed by Internovi, Cesena, Italy).

### *Risk of bias across studies*

Publication bias was assessed both visually by a funnel plot

		Bliss et al.	Glinkowski et al.	Hebal et al.	Poncet et al.	Uccheddu et al.
1. Research question						
A.	The research question, objective(s) and/or hypotheses were clearly stated	Yes	Yes	Yes	Yes	Yes
2. Study population						
A.	The source population was clearly defined	No	Yes	Yes	Yes	Yes
B.	All subjects were selected or recruited from the same or similar population(s)	NR	NR	Yes	Yes	Yes
C.	Inclusion and/or exclusion criteria were clearly defined	No	No	Yes	Yes	Yes
3. Study design						
A.	The study design was stated to be prospective	NR	Yes	Yes	Yes	Yes
B.	The participation rate of eligible persons was at least 50%	NR	NR	Yes	NR	NR
4. Measurements, analyses and outcomes						
A.	Method(s) of measurement(s) were clearly defined	Yes	Yes	Yes	Yes	Yes
B.	Used soft- and hardware were clearly described	Yes	Yes	Yes	Yes	Yes
C.	Measurements were performed in a valid, blinded, and/or standardized manner	Yes	Yes	Yes	Yes	Yes
D.	Methods of statistical analyses were clearly described and appropriate	Yes	Yes	Yes	Yes	No
E.	Data presentation included measures of precision (e.g. SD or range)	NR	Yes	Yes	Yes	Yes
F.	Outcome data were available for (nearly) all participants (max. loss = 20% after baseline)	Yes	Yes	Yes	Yes	No
5. Overall quality judgement		Fair	Good	Good	Good	Fair

**Figure 1** Risk of bias per individual study. NR, not reported.

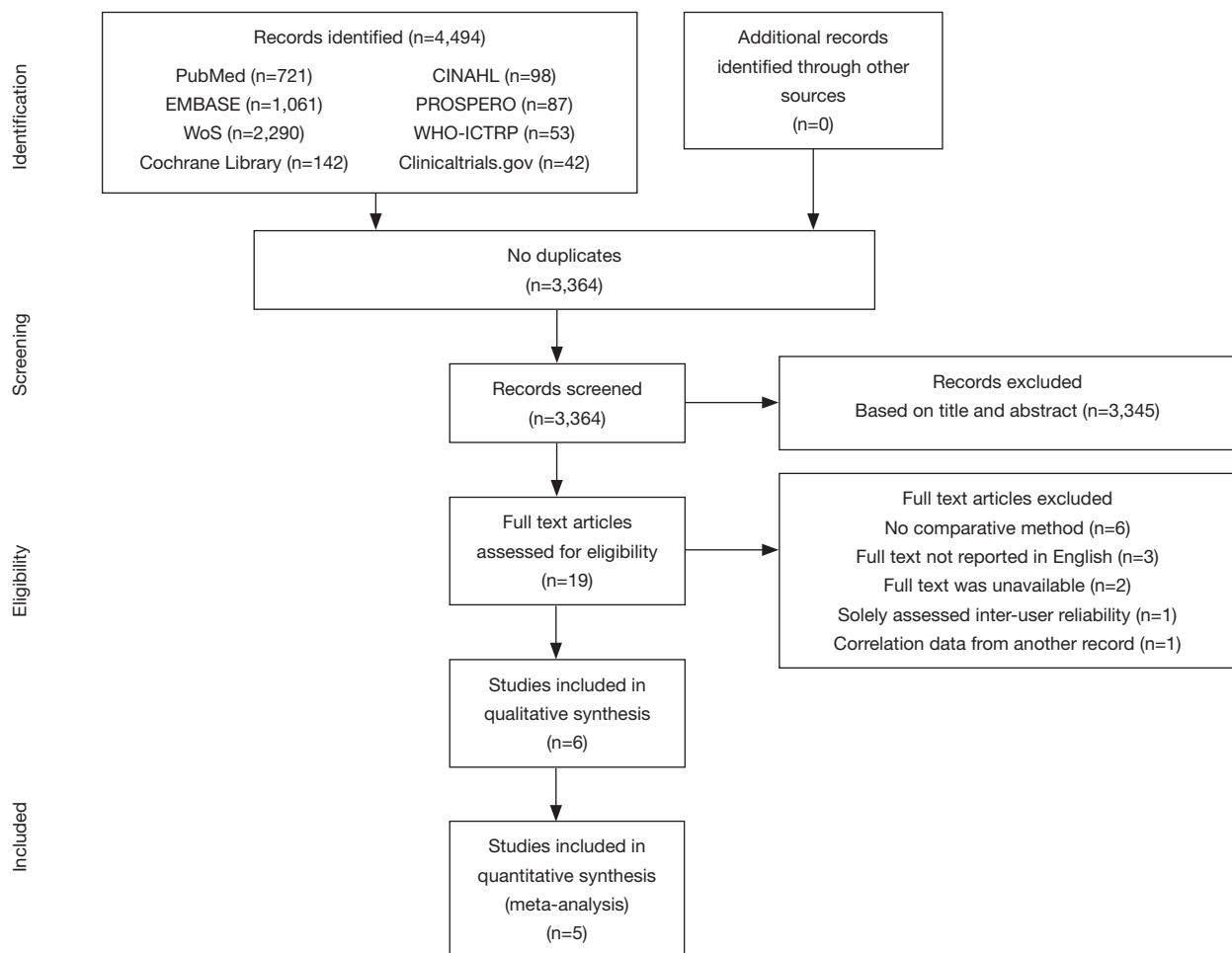
(a standard error by Z-score plot of the primary outcome measure), and statistically with Egger's linear regression, and Begg's and Mazumdar's rank correlation tests. A P value  $\leq 0.10$  was considered statistically significant. Publication bias analyses were performed by ProMeta 3.0 software for MacOS (based on ProMeta 2.1, deployed by Internovi, Cesena, Italy).

## Results

### Study selection

See flow diagram, *Figure 2*. The PubMed (n=721), EMBASE (n=1,061), Web of Science (n=2,290), Cochrane Library (n=142), CINAHL (n=98), PROSPERO (n=87), WHO-ICTRP (n=53), and Clinicaltrials.gov (n=42) databases and registries provided a total number of 4,494

citations. No citations were obtained through the related-articles and cross-reference searches. No unpublished data was obtained. Of the 4,494 citations, 1,130 duplicates were discarded using the Mendeley find duplicates function (Mendeley Desktop v1.19.4 for MacOS, Mendeley Ltd., Elsevier). An additional 3,345 studies were discarded because their title and/or abstract did not comply with the predetermined eligibility criteria. Full texts of the remaining 19 papers were read, whereupon another 14 papers were excluded for systematic review. Reasons for exclusion were: lack of a comparative method (n=6); the full text was NR in the English language (n=3); only a conference abstract was available (n=2); the fact that only inter-user reliability was assessed (n=1); PE and PC data were not presented separately (n=1) or the use of correlation data from another article (n=1). Eventually, 5 papers were considered eligible



**Figure 2** A PRISMA flow diagram of the study selection procedure. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; WoS, Web of Science; CINAHL, Cumulative Index to Nursing and Allied Health Literature; WHO-ICTRP, World Health Organization International Clinical Trials Registry Platform.

for systematic review and qualitative synthesis, while 4 papers were also included for quantitative synthesis (i.e., meta-analysis).

### Study characteristics

#### Methods

See *Table 1*. All included papers conducted an observational study, of which 4 were stated to be prospective (14-17). No randomized controlled trials were included. Studies were conducted in Canada, Italy, Poland, Spain or the USA, participants were enrolled between 2005 and 2017.

#### Participants

In total, 75 participants were enrolled. All studies included

participants with PE whereas the study performed by Poncet *et al.* (16) was the only study to also include 5 participants with PC (*Table 1*). This study was not excluded because PE and PC data were reported separately. The percentage of male subjects with PE ranged from 80% to 100%, as reported by Bliss *et al.* (18) and Glinkowski *et al.* (14). Individual sample sizes ranged from 4 to 39 participants. The mean age of participants with PE was reported by Bliss *et al.* (18), Glinkowski *et al.* (14) and Poncet *et al.* (16) and ranged from 13.8 to 16.5 years. The mean age of participants with PC was 11.6 (SD: 4.5) years (16).

#### Intervention

##### 3D thoracic surface scan

See *Tables 2,3*. All studies utilized 3D scanners of different

**Table 1** Study and patient characteristics

Author	Country	Study design	Study period	Study size	Chest wall deformity studied	Age (years), mean (SD)	Male, n (%)
Bliss <i>et al.</i>	USA	Observational study	28 months	10	PE	16.5 (2.2)	8 (80.0)
Glinkowski <i>et al.</i>	Poland	Prospective observational study	November 2007–December 2008	12	PE	16 (5.0)	12 (100.0)
Hebal <i>et al.</i>	USA	Prospective observational study	April 2015–April 2017	39	PE	NR	NR
Poncet <i>et al.</i>	Canada	Prospective observational study	July 2005–March 2006	5	PE	13.8 (1.5)	NR
				5	PC	11.6 (4.5)	NR
Uccheddu <i>et al.</i>	Italy	Prospective observational study	NR	4	PE	NR	NR

PE, pectus excavatum; PC, pectus carinatum; SD, standard deviation.

**Table 2** Acquisition characteristics

Author	3D-scanner	Static, handheld, or mounted	3D-scanning method	Accuracy, mm	Patient position	Respiratory phase	Acquisition range, degrees	Duration of acquisition, seconds	Duration of reconstruction, minutes
Bliss <i>et al.</i>	3dMD torso photography system (3dMD LLC, Atlanta, GA, USA)	Static	Structured light	NR	Upright, standing position with arms in a T-pose position	NR	360	Several milliseconds	NR
Glinkowski <i>et al.</i>	Self-built scanner that consisted of MT700 projectors (Toshiba, Minato, Tokyo, Japan) and Flea B&W cameras (Point Grey Research Inc., Richmond, Canada)	Static	Structured light	0.2–0.4	Upright, standing position	Holding breath	360	0.7	NR
Hebal <i>et al.</i>	Rodin M4D (Rodin4d, Mérignac, France)	Handheld	Structured white light	NR	Upright, standing position with shoulders abducted 45°	During expiration	360	180	5–10 <sup>a</sup>
Poncet <i>et al.</i>	InSpeck (InSpeck Inc., Montreal, Quebec, Canada)	Static	Structured white light	0.006	Upright, standing position with arms above shoulders.	NR	360	<24	NR
Uccheddu <i>et al.</i>	Microsoft Kinect v2 (Microsoft, Redmond, WA, USA)	Mounted but translatable	Structured light	NR	Supine position on a semirigid mattress	Holding breath, following expiration	Frontal acquisition only	<1	NR

<sup>a</sup>, duration for the entire scanning process (acquisition & reconstruction), with often multiple acquisitions being needed. 3D, three-dimensional; NR, not reported.

Table 3 Measurement characteristics

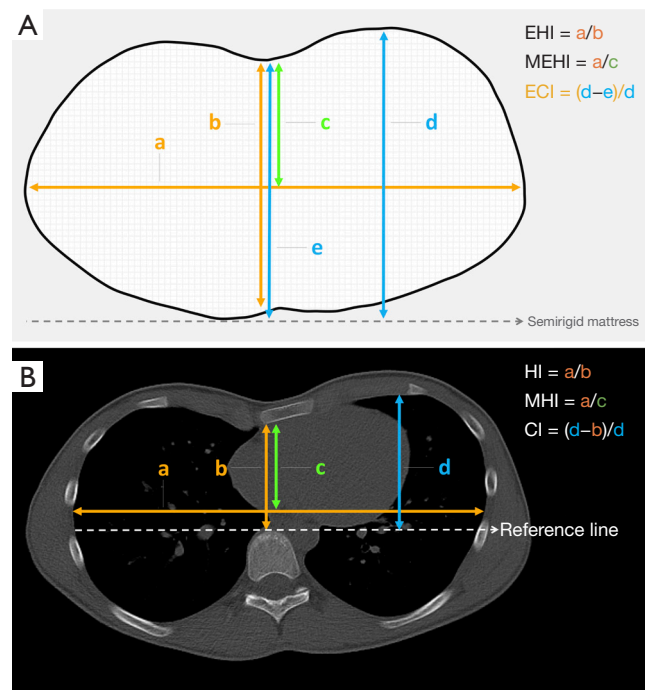
Author	Software used for 3D-scan measurements	Chest wall deformity studied	3D-scan measurement method (Figure 3A)	Measured 3D value, mean (SD; range)	Method of reference	Reference measurement method (Figure 3B)	Measured reference value, mean (SD; range)	Correlation, correlation coefficient	P value
Bliss <i>et al.</i>	3dMDvultus (3dMD LLC, Atlanta, Georgia, USA)	PE	EHI	NR	CT	Conventional HI	3.67 (0.92; 2.44–5.60)	$r^2=0.76$ ; $r=0.87$	0.001 <sup>a</sup>
		PE	Pectus Surface Area Ratio	NR	CT	Conventional HI	3.67 (0.92; 2.44–5.60)	$r^2=0.46$ ; $r=0.68$	0.03 <sup>a</sup>
		PE	Pectus Volume Ratio	NR	CT	Conventional HI	3.67 (0.92; 2.44–5.60)	$r^2=0.30$ ; $r=0.58$	0.1
Glinkowski <i>et al.</i>	Self-developed	PE	EHI	1.84 (0.11; 1.70–2.13)	CT	Conventional HI	3.82 (0.17; 3.58–4.22)	$r^2=0.87$ ; $r=0.93$	<0.001 <sup>a</sup>
		PE	EHI	1.84 (0.11; 1.70–2.13)	CT	EHI	1.93 (0.13; 1.77–2.24)	$r^2=0.99$ ; $r=0.99$	<0.001 <sup>a</sup>
Hebal <i>et al.</i>	NR	PE	EHI	NR	CT	Conventional HI	NR	$r=0.87$	<0.001 <sup>a</sup>
Poncet <i>et al.</i>	InSpeck (InSpeck Inc., Montreal, Quebec, Canada)	PE	EHI	2.06 (0.46; 1.72–2.82)	CT	Conventional HI	4.28 (1.40; 3.00–6.00)	$r=0.92$	0.03 <sup>a</sup>
		PE	MEHI	5.29 (3.45; 3.09–11.23)	CT	Modified Conventional HI	11.33 (8.07; 5.34–24.00)	$r=0.97$	0.006 <sup>a</sup>
		PC	EHI	1.28 (0.15; 1.07–1.47)	CT	Conventional HI	1.66 (0.39; 1.19–2.20)	$r=0.88$	0.049 <sup>a</sup>
		PC	MEHI	1.81 (0.29; 1.33–2.07)	CT	Modified Conventional HI	2.55 (0.34; 2.27–3.10)	$r=0.44$	0.5
Uccheddu <i>et al.</i>	Self-developed	PE	EHI	17.50% (6.25%; 10–25%)	CT	Conventional correction index	17.00% (6.48%; 9–24%)	$r=0.99$	0.01 <sup>a</sup>

<sup>a</sup>, statistically significant ( $P \leq 0.05$ ). 3D, three-dimensional; PE, pectus excavatum; PC, pectus carinatum; SD, standard deviation; NR, not reported; CT, computed tomography; EHI, external Haller index; MEHI, modified external Haller index; ECI, external correction index; HI, Haller index.

manufacturers. Three studies used a static scanner type (14,16,18), while Hebal *et al.* (15) used a handheld scanner and Uccheddu *et al.* (17) mounted their scanner on a specially devised frame that allowed vertical translation. Despite these differences, all scanners used structured (white) light projectors to detect the 3D thoracic surface. Prior to acquisition, 4 studies (14–16,18) positioned their participants in an upright standing position with the arms at the level of, or above the shoulders. The same 4 studies all acquired a 360° thoracic surface scan. In contrast, Uccheddu *et al.* (17) positioned their participants in a supine position on a semi rigid mattress and solely obtained a frontal acquisition. Among the reported studies, scans were all acquired at different phases of the respiratory cycle (14,15,17). Acquisition of the 3D scans took several milliseconds to 180 seconds whereas reconstruction took up to 10 minutes (15,18). Scanner accuracy was reported to

be 0.2–0.4 mm. for the study of Glinkowski *et al.* (14) and 0.006 mm. for Poncet *et al.* (16).

In four studies thoracic surface scan-based PE severity measurements were calculated by dividing the widest external thoracic transverse diameter by the distance between the external vertebral body and external deepest point (Figure 3A) (14–16,18). Terminology of this measure differed among all four studies but will from this point on be referred to as the external Haller index (EHI). Bliss *et al.* (18) additionally derived two, self-developed PE measures: The Pectus Volume Ratio and Surface Area Ratio. The latter was obtained by calculating the ratio between the surface area of both the chest deformity (i.e., the area beneath the normal aspect of the anterior chest) and torso (i.e., sternal notch to xiphoid). The same applies to the Volume Ratio, for which volumes were used. In addition, Poncet *et al.* (16) also reported another self-developed PE measure that



**Figure 3** Pectus severity measurement methods.. (A) Severity indices based on 3D surface scans; (B) severity indices based on CT-scans. EHI, external Haller index; MEHI, modified external Haller index; ECI, external correction index; HI, Haller index; MHI, modified Haller index; CI, correction index; 3D, three-dimensional.

was modified from the EHI; the modified external Haller index (MEHI) (Figure 3A). This measure was calculated by dividing the widest external thoracic transverse diameter by the anteroposterior distance from the imaginary transverse diameter line to the external deepest point. Uccheddu *et al.* (17) only calculated the external Correction index (ECI) (Figure 3A), that is defined as:  $(d-e)/d$ , where  $d$  and  $e$  are the vertical distances of, respectively, the minimum and maximum sternal depression with respect to the reference plane (i.e., the semirigid mattress plane).

To determine the severity of PC, Poncet *et al.* (16) utilized similar measures as for PE, however, for PC the point of maximal protrusion was used as reference point.

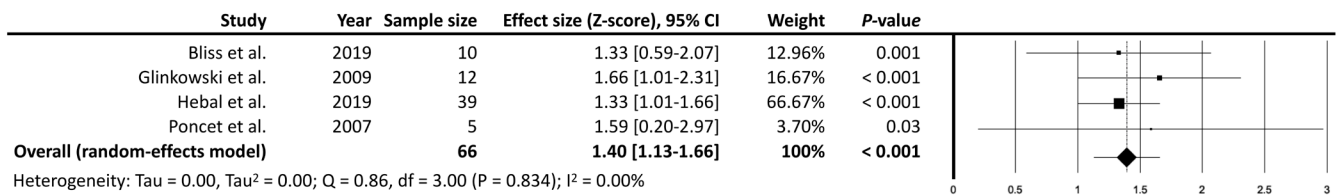
### Comparison

See Table 3. To assess 3D surface scan performance, all studies acquired a comparative thoracic CT-scan (14-18); the current gold standard for pectus severity quantification. All studies analyzed thoracic surface and CT-scan based measurements of the same participant. In comparison to the aforementioned 3D scan measures, CT-scan derived severity measurements were based on internal diameters. Four out of 5 studies calculated the conventional HI (Figure 3B)

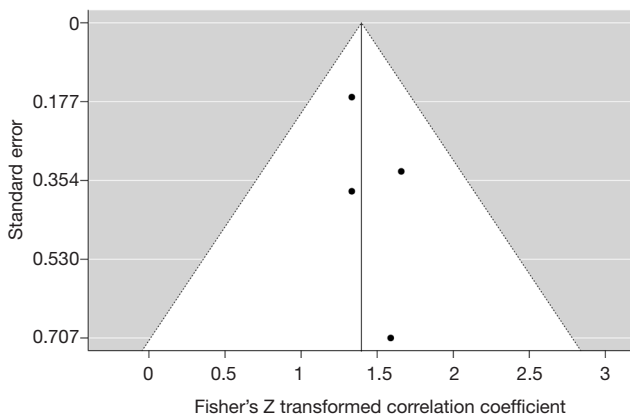
to determine PE severity (14-16,18). The HI was obtained by dividing the widest inner thoracic diameter by the anteroposterior distance from the posterior sternal surface to the anterior vertebral surface. Glinkowski *et al.* (14) additionally derived the CT-based EHI to assess 3D and CT-scan agreement. In line with the aforementioned thoracic surface scan indices, Poncet *et al.* (16) reported an additional, self-developed modified Haller index (MHI) (Figure 3B), obtained by dividing the widest internal transverse diameter by the anteroposterior distance from the imaginary widest internal transverse diameter line to the posterior sternal surface. In comparison, Uccheddu *et al.* (17) used the Correction index to determine the CT-based PE severity. This index measures the percentage of PE to be corrected and is calculated by the following formula (Figure 3B):  $(d-b)/d$ , where  $d$  and  $b$  are the vertical distances of, respectively, the minimum and maximal sternal depression with respect to the anterior vertebral body reference line.

To determine the CT-based PC severity, Poncet *et al.* (16) again utilized similar measures as for PE, however, for PC the point of maximal protrusion was used as point of reference.





**Figure 4** Meta-analysis demonstrating the correlation of 3D optical surface scan based EHI and CT-scan based HI among participants with pectus excavatum, using Fisher's Z-score as effect size. CI, confidence interval; 3D, three-dimensional; CT, computed tomography; EHI, external Haller index; HI, Haller index.



**Figure 5** A standard error by Fisher's Z transformed correlation coefficient to detect the presence of publication bias among the studies that were included for quantitative synthesis.

## Outcomes

One paper compared its thoracic surface and CT-scan derived pectus severity measurements using the Pearson's correlation coefficient ( $r$ ) (15) while two studies reported the squared variant ( $r^2$ ) (14,18). Uccheddu *et al.* (17) reported the raw outcome data only, whereas Poncet *et al.* (16) reported correlation data for their entire study population (i.e., PE and PC combined) including the raw data. The level of statistical significance was only denoted by Hebal *et al.* (15). Missing correlation coefficients and P values were calculated post hoc.

## Risk of bias within studies

See *Figure 1* for the risk of bias assessment per study. The study of Glinkowski *et al.* (14), Hebal *et al.* (15) and Poncet *et al.* (16) were all judged to be of good methodological quality; i.e., outcome measures were not doubted. The study of Bliss *et al.* (18) and Uccheddu *et al.* (17) were considered

to be of fair methodological quality.

## Synthesis of results

### Qualitative synthesis

See *Table 3*. For PE, correlation sizes ( $r$ ) ranged from 0.87 to 0.93 among studies that assessed the correlation of 3D scan derived EHI and CT-scan derived HI (14-16,18). These correlations were all statistically significant. The size of correlation was not affected by the type of 3D scanner used, although the use of a handheld scanner was associated with a prolonged acquisition time. Bliss *et al.* (18) additionally determined their self-developed 3D scan based Pectus Surface Area Ratio and Pectus Volume Ratio and assessed its agreement to the conventional CT-based HI. They found moderate positive correlations of 0.68 ( $P=0.03$ ) and 0.58 ( $P=0.1$ ), respectively. In a similar manner, Glinkowski *et al.* (14) assessed the correlation of the 3D- and CT-scan derived EHI and found a coefficient of 0.99 ( $P<0.001$ ); suggesting near perfect agreement between both acquisitions. Poncet *et al.* (16) additionally assessed the correlation of their self-constructed MHI and MEHI that was respectively obtained from acquired CT- and 3D-scans of participants with PE. Correlation of these modified indices ( $r=0.98$ ;  $P<0.001$ ) was slightly superior to the correlation of the 3D-EHI and CT-scan derived HI ( $r=0.96$ ;  $P<0.001$ ). However, superiority of the 3D scan derived MEHI over the EHI remains unknown, while the MEHI was not compared to the gold standard (i.e., CT derived HI). Uccheddu *et al.* (17) quantified PE severity utilizing the 3D-derived ECI and CT-scan derived CI, and found a correlation coefficient of 0.99 ( $P=0.01$ ).

As mentioned in the previous sections, Poncet *et al.* (16) also investigated the correlation of the 3D scan derived EHI and MEHI with the CT-based conventional HI and MHI to determine the severity of PC. They found a high and low

correlation of 0.88 ( $P=0.049$ ) and 0.44 ( $P=0.5$ ), respectively.

### Quantitative synthesis

The study of Bliss *et al.* (18), Glinkowski *et al.* (14), Hebal *et al.* (15) and Poncet *et al.* (16) were found to be sufficiently homogenous to be admitted for quantitative synthesis because they all included patients with PE and utilized identical severity metrics. From the study of Poncet *et al.* (16), only participants with PE were included for quantitative synthesis. Inspection of the individual correlation coefficients and forest plot (*Figure 4*) indicated the presence of an overall high positive correlation between the CT-based HI and 3D scan-based EHI. This was statistically confirmed by meta-analysis (*Figure 4*) that demonstrated a pooled Z-score of 1.40 (95% CI: 1.13 to 1.66;  $P<0.001$ ) These Z-scores corresponded with a pooled correlation coefficient of 0.89 (95% CI: 0.81 to 0.93;  $P<0.001$ ). No heterogeneity was detected ( $I^2=0.00\%$ ;  $P=0.834$ ). No subgroup analyses were performed.

### Risk of bias across studies

A funnel plot of the studies that were included for quantitative synthesis was constructed. Graphical assessment demonstrated no evident asymmetry; indicating the absence of publication bias (*Figure 5*). This was statistically reproduced by Begg's and Mazumdar's rank correlation test ( $P=0.497$ ) and by Egger's linear regression test ( $P=0.407$ ).

### Discussion

This systematic review and meta-analysis examined all studies that compared the use of 3D optical imaging and CT-scans or chest radiographies in the quantification of pectus severity. Based on the previously described eligibility criteria, 5 observational studies were included, enrolling a total of 75 participants. Of these, 70 were participants with PE. No studies were judged to be of poor methodological quality. No studies were included that assessed the use of two-view plain radiographies. All studies utilized CT-scan based severity metrics as comparison; the current gold standard for severity quantification. To assess 3D- and CT-scan agreement, all studies calculated correlation coefficients or correlation coefficients could be determined from the available raw data. Only one of these studies investigated the correlation among participants with PC (16). This low number of studies describing the use of 3D scans to determine PC severity may be a direct consequence of

the absence of a standardized PC severity measure. Among participants with PC ( $n=5$ ), Poncet *et al.* (16) found a high correlation of 0.88 between the CT-based HI and 3D-based EHI with a 95% CI that ranged from  $-0.01$  to  $0.92$ . We subsequently concluded that with the currently available limited data no evidence can be produced to either support nor discard the use of 3D scans to determine PC severity in comparison to CT-scans and chest radiographies. Nevertheless, 3D scans may be used to monitor treatments such as compressive orthotic bracing as described by Wong *et al.* (19).

Four out of five included studies acquired identical 3D scan and CT derived PE severity indices and were subjected to meta-analysis. Pooled analysis revealed a high positive, statistically significant correlation between the optical scan measured EHI and CT-scan derived conventional HI ( $r=0.89$ ;  $P<0.001$ ). Although pooled analysis demonstrated a high correlation, 3D thoracic surface scan derived External Haller indices are not yet a valid tool to aid in the multifactorial process of surgical decision making. Correlation coefficients express the direction and magnitude of a linear relationship between two measures, but they do not assess their exact agreement. This is best illustrated by Glinkowski *et al.* (14) and Poncet *et al.* (16) who found mean 3D scan-based EHI values of 1.84 and 1.67, with corresponding mean CT-based HI values of 3.82 and 2.97. Based on these means, fewer patients would have been operated on the basis of the 3D measurements, in comparison to CT if the same cut-off values would have been used. Consequently, for the 3D scan EHI to be used in the process of decision-making new threshold values should be determined. To date, no such studies exist.

The study of Ucheddu *et al.* (17) compared the 3D scan derived ECI and the CT-scan based correction index, and found similar mean index values 17.50% (SD: 6.25%; range: 10–25%) *vs.* 17.00% (SD: 6.48%; range: 9–24%) with a correlation coefficient of 0.99. One may subsequently assume that both imaging modalities can be used interchangeably to determine the (external) correction index. However, the power of evidence is low with only 4 included participants, therefore more data are needed to be able to draw a definite conclusion.

The novel 3D scan-based Pectus Surface Area Ratio and Volume Ratio that were introduced by Bliss *et al.* (18) demonstrated only moderate correlations with the conventional HI. This may be due to the fact that the HI is calculated from a single plane that exhibits the maximum depression. Yet, pectus morphologies are not restricted to a

two-dimensional plane but are rather multiplanar. The HI is, moreover, dependent of the shape of the thorax. This means that a certain pectus depth results in different indices if the chest is for example flat or barrel shaped. In the past years, several alternative metrics have been proposed to better describe the extent of PE deformities, however, their clinical use remains uncertain. Until now, the HI is still considered the reference standard for research purposes and reimbursement decisions. Nevertheless, considerations to determine surgical therapy are multifactorial and vary widely among institutions around the world. In our opinion indices should not be used as a hard criterion to determine surgical candidacy or its reimbursement but be part of the multifactorial decision wherein more attention is given to physiological symptoms such as cardiac and pulmonary impairment. To quantify cardiac function one may for example use the cardiac index, which was investigated by Maagaard *et al.* (4) and shown to increase following minimally invasive PE repair.

One of the main disadvantages of 3D scanning versus cross-sectional imaging is the missing intrathoracic anatomical information, such as sternal torsion and (cardio) pulmonary impression. However, as the majority of cases are not severe, they do not necessarily require cross-sectional imaging and a 3D optical image would suffice. Additional cross-sectional imaging could then be reserved for severe cases that are suspected for intrathoracic anomalies of the underlying heart and lungs. Cardiopulmonary impairment may also be assessed functionally by e.g., an electrocardiogram (ECG), echocardiography and spirometry, but their relation to cross-sectional imaging is yet to be investigated. Hypothetically, such diagnostics may even outperform conventional cross-sectional imaging as it provides dynamic information on (cardio) pulmonary functioning. For example, heart valve diseases and pulmonary function can neither be assessed by CT nor plain radiography nor with a 3D scan. It should subsequently be advised to offer functional tests such as ECG, echocardiography and spirometry or body plethysmography as adjunct methods to the standard preoperative panel, regardless of the imaging technique used to determine pectus severity. Another limitation is that 3D scans rely on body constitution. Measures in obese and female (because of the mammae) patients may subsequently differ from thin and male patients. Nevertheless, in contrast to cross-sectional images, 3D scans can be repeated endlessly without exposure to ionizing radiation. In most centers, 3D optical scanners are not available, whereas

the vast majority features equipment to acquire CT-scans and plain radiographies. However, a reduction in exposure to radiation may easily justify the one-time costs of a 3D scanner.

During the respiratory cycle, chest dimensions are dynamic with the minimum anteroposterior diameter being achieved following full expiration. At this point, the external and internal HI [i.e., (E)HI] are maximum, as also found by Birkemeier *et al.* (20) and Albertal *et al.* (21) who, moreover, reported PE severity indices to be significantly more severe at end-expiration. In this review, only Uccheddu *et al.* (17) acquired their 3D scans at end-expiration. In addition, no studies reported the respiratory phase in which the CT was acquired. Reported index values may subsequently be an underestimation.

None of the included studies compared their 3D scan severity measurements to those based on chest radiographies. Still, standard two-view chest radiographies are commonly acquired in the daily work- and follow-up of pectus patients and serve as a valid alternative to CT-scans (22). Despite a reduction in dose compared to CT, chest radiographies still require exposure to radiation that is associated with long-term side effects ranging from growth derangements to malignancies (6,7). Following similar dogmas of minimization of radiation exposure and its potential harm, chest radiographies should ideally be replaced by a radiation free imaging method, such as 3D optical surface scanning. MRI could also serve as a radiation free alternative to radiographies and CT-scans. Its feasibility has already been demonstrated by Birkemeier *et al.* (23), while Lo Piccolo and colleagues (24) even found comparable severity values, comparing MRI and CT-scans. However, MRI is generally associated with increased costs, reduced availability, is more time-consuming, difficult to perform in claustrophobic patients, motion sensitive, and requires sedation in young patients, making it a less attractive alternative (23,24).

In conclusion, 3D optical scanning is an attractive, feasible and promising imaging technique to determine the severity of PE without exposure to ionizing radiation. No evidence was found that supports nor discards the use of 3D scans to determine PC severity. Meta-analytical review of participants with PE demonstrated a pooled correlation of 0.89 between the CT derived HI and its 3D scan equivalent based on external measures. However, despite this high correlation, further research is imperative for 3D scans to be used in the clinical process of decision making and help determine surgical candidacy.

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## Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd.2020.02.31>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Supplementary

Overview		
Interface	PubMed.com	
Date of search	April 30 <sup>th</sup> , 2019	
Number of results	721	
Syntax guide		
Mesh	Medical subject headings	
Mesh:NoExp	Medical subject headings without explosion	
tiab	Words in title or abstract	
*	Truncation	
Search	Query	Items found
#1	“funnel chest”[Mesh]	2,301
#2	funnel chest*[tiab] OR pectus excavatum*[tiab] OR funnel breast*[tiab] OR chonechondrosternon[tiab] OR funnel thorax[tiab] OR foveated chest*[tiab] OR foveated thorax[tiab] OR koilosternia[tiab]	25,89
#3	“pectus carinatum”[Mesh]	85
#4	pectus carinatum*[tiab] OR pouter pigeon breast*[tiab] OR pigeon chest*[tiab] OR pigeon breast*[tiab] OR pouter breast*[tiab] OR pigeon thorax[tiab]	584
#5	“sternum”[Mesh]	9,019
#6	sternum*[tiab]	6,663
#7	“thoracic wall”[Mesh]	4,034
#8	thorax wall*[tiab] OR thoracic wall*[tiab] OR chest wall*[tiab]	18,256
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	33,053
#10	“imaging, three-dimensional”[Mesh:NoExp]	65,671
#11	3 D Imag*[tiab] OR three dimensional imag*[tiab] OR optic*[tiab] OR 3D imag*[tiab] OR threedimensional imag*[tiab] OR three dimensional reconstructi*[tiab] OR three-dimensional reconstructi*[tiab] OR 3 D scan*[tiab] OR three dimensional scan*[tiab] OR 3D scan*[tiab] OR threedimensional scan*[tiab] OR white light*[tiab] OR structured light*[tiab] OR laser*[tiab] OR body scan*[tiab] OR body imag*[tiab] OR torso scan*[tiab] OR torso imag*[tiab] OR modulated light*[tiab] OR torso topograp*[tiab]	608,365
#12	#10 OR #11	661,332
#13	#9 AND #12	721

Figure S1 PubMed.

Overview		
Interface	EMBASE.com	
Date of search	April 30 <sup>th</sup> , 2019	
Number of results	1,061	
Syntax guide		
/exp	EMtree keyword with explosion	
/de	EMtree keyword without explosion	
:ab,ti	Words in title or abstract	
*	Truncation	
Search	Query	Items found
#1	'funnel chest'/exp	3,661
#2	'pigeon thorax'/exp	983
#3	'thorax wall'/exp	12,946
#4	'chest wall*':ab,ti OR 'thorax wall*':ab,ti OR 'thoracic wall*':ab,ti	25,818
#5	'chicken breast*':ab,ti OR 'pectus carinatum*':ab,ti OR 'pectus carinatus':ab,ti OR 'pigeon breast*':ab,ti OR 'pigeon thorax':ab,ti OR 'pigeon chest*':ab,ti OR 'pouter breast*':ab,ti OR sternum*:ab,ti	10,064
#6	'funnel breast*':ab,ti OR 'funnel chest*':ab,ti OR chonechondrosternon:ab,ti OR 'foveated chest*':ab,ti OR 'foveated thorax':ab,ti OR 'funnel thorax':ab,ti OR koilosternia:ab,ti OR 'pectus excavatum':ab,ti	3,120
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	40,180
#8	'white light'/exp	3,635
#9	'three dimensional imaging'/de	85,213
#10	'three-dimensional imag*':ab,ti OR 'three dimensional imag*':ab,ti OR 'three dimensional reconstructi*':ab,ti OR 'three-dimensional reconstructi*':ab,ti OR '3 d imag*':ab,ti OR optic*:ab,ti OR '3d imag*':ab,ti OR 'threedimensional imag*':ab,ti OR '3 d scan*':ab,ti OR 'three dimensional scan*':ab,ti OR '3d scan*':ab,ti OR 'threedimensional scan*':ab,ti OR 'white light*':ab,ti OR 'structured light*':ab,ti OR laser*:ab,ti OR 'body scan*':ab,ti OR 'body imag*':ab,ti OR 'torso scan*':ab,ti OR 'torso imag*':ab,ti OR 'modulated light*':ab,ti OR 'torso topograp*':ab,ti	599,282
#11	#8 OR #9 OR #10	666,938
#12	#7 AND #11	1,061

**Figure S2** EMBASE.

Overview		
Interface	Web of Science/Clarivate Analytics	
Date of search	April 30 <sup>th</sup> , 2019	
Number of results	2,290	
Syntax guide		
*	Truncation	
Search	Query	Items found
#1	<p>TOPIC: (funnel breast* OR funnel chest* OR chonechondrosternon OR foveated chest* OR foveated thorax OR funnel thorax OR koilosternia OR pectus excavatum OR chicken breast* OR pectus carinatum* OR pectus carinatus OR pigeon breast* OR pigeon thorax OR pigeon chest* OR pouter breast* OR sternum* OR chest wall* OR thorax wall* OR thoracic wall*)</p> <p>Indexes=SCI-EXPANDED, SSCI, A&amp;HCI, ESCI Timespan=All years</p>	35,752
#2	<p>TOPIC: (three-dimensional imag* OR three dimensional imag* OR three dimensional reconstructi* OR three-dimensional reconstructi* OR 3 d imag* OR optic* OR 3d imag* OR threedimensional imag* OR 3 d scan* OR three dimensional scan* OR 3d scan* OR threedimensional scan* OR white light* OR structured light* OR laser* OR body scan* OR body imag* OR torso scan* OR torso imag* OR modulated light* OR torso topograp*)</p> <p>Indexes=SCI-EXPANDED, SSCI, A&amp;HCI, ESCI Timespan=All years</p>	2,277,572
#3	#1 AND #2 Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years	2,290

**Figure S3** Web of Science.



Overview		
Interface	Cochrane Library/Wiley	
Date of search	April 30 <sup>th</sup> , 2019	
Number of results	142 (Cochrane reviews: 2; Trials: 140)	
Syntax guide		
ti,ab,kw	Words in title, abstract or author keywords	
*	Truncation	
Search	Query	Items found
#1	(funnel breast* OR funnel chest* OR chonechondrosternon OR foveated chest* OR foveated thorax OR funnel thorax OR koilosternia OR pectus excavatum OR chicken breast* OR pectus carinatum* OR pectus carinatus OR pigeon breast* OR pigeon thorax OR pigeon chest* OR pouter breast* OR sternum* OR chest wall* OR thorax wall* OR thoracic wall*):ti,ab,kw	2,569
#2	(three-dimensional imag* OR three dimensional imag* OR three dimensional reconstructi* OR three-dimensional reconstructi* OR 3 d imag* OR optic* OR 3d imag* OR threedimensional imag* OR 3 d scan* OR three dimensional scan* OR 3d scan* OR threedimensional scan* OR white light* OR structured light* OR laser* OR body scan* OR body imag* OR torso scan* OR torso imag* OR modulated light* OR torso topograp*):ti,ab,kw	45,883
#3	#1 AND #2	142

**Figure S4** Cochrane Library.

Overview		
Interface	CINAHL/EBSCOhost	
Date of search	April 30 <sup>th</sup> , 2019	
Number of results	98	
Syntax guide		
TI	Words in title	
AB	Words in abstract	
*	Truncation	
Search ID#	Query	Items found
S1	TI (funnel breast* OR funnel chest* OR chonechondrosternon OR foveated chest* OR foveated thorax OR funnel thorax OR koilosternia OR pectus excavatum OR chicken breast* OR pectus carinatum* OR pectus carinatus OR pigeon breast* OR pigeon thorax OR pigeon chest* OR pouter breast* OR sternum* OR chest wall* OR thorax wall* OR thoracic wall*)	1,250
S2	AB (funnel breast* OR funnel chest* OR chonechondrosternon OR foveated chest* OR foveated thorax OR funnel thorax OR koilosternia OR pectus excavatum OR chicken breast* OR pectus carinatum* OR pectus carinatus OR pigeon breast* OR pigeon thorax OR pigeon chest* OR pouter breast* OR sternum* OR chest wall* OR thorax wall* OR thoracic wall*)	3,143
S3	S1 OR S2	3,797
S4	TI (three-dimensional imag* OR three dimensional imag* OR three dimensional reconstructi* OR three-dimensional reconstructi* OR 3 d imag* OR optic* OR 3d imag* OR threedimensional imag* OR 3 d scan* OR three dimensional scan* OR 3d scan* OR threedimensional scan* OR white light* OR structured light* OR laser* OR body scan* OR body imag* OR torso scan* OR torso imag* OR modulated light* OR torso topograp*)	22,666
S5	AB (three-dimensional imag* OR three dimensional imag* OR three dimensional reconstructi* OR three-dimensional reconstructi* OR 3 d imag* OR optic* OR 3d imag* OR threedimensional imag* OR 3 d scan* OR three dimensional scan* OR 3d scan* OR threedimensional scan* OR white light* OR structured light* OR laser* OR body scan* OR body imag* OR torso scan* OR torso imag* OR modulated light* OR torso topograp*)	39,431
S6	S5 OR S6	50,625
S7	S3 AND S6	98

**Figure S5** CINAHL.