
Article:
Digby, M.G., Bishop, N.J. orcid.org/0000-0001-7263-8546, Paggiosi, M.A. et al. (1 more author) (2016) HR-pQCT: a non-invasive 'biopsy' to assess bone structure and strength. Archives of Disease in Childhood.education and Practice Edition , 101 (5). pp. 268-270. ISSN 1743-0585

https://doi.org/10.1136/archdischild-2015-309455

HR-pQCT: A Non-Invasive "Biopsy" to Assess Bone Structure and Strength

Authors: Digby MG[1], Bishop NJ[2], Paggiosi MA[3], Offiah AC[2]

1. Sheffield Medical School, University of Sheffield UK
2. Academic Unit of Child Health, University of Sheffield UK
3. Mellanby Centre for Bone Research, University of Sheffield UK

Corresponding Author:

Dr Amaka C Offiah BSc, MBBS, MRCP, FRCR, PhD, FHEA
Reader in Paediatric Musculoskeletal Imaging
University of Sheffield
Academic Unit of Child Health,
Room C4, Stephenson Wing,
Sheffield Children's NHS Foundation Trust,
Western Bank,
Sheffield,
S10 2TH.

Phone: 0114 271 7557
Fax: 0114 2755364
a.offiah@sheffield.ac.uk

Five key words
HR-pQCT
Bone health
Paediatrics
Imaging
Technology

HR-pQCT: A Non-Invasive "Biopsy" to Assess Bone Structure and Strength

Introduction

One third of children will sustain a fracture by the age of 17 years, and 25-35% of these will be of the distal forearm. There is evidence that childhood fractures are linked to underlying skeletal fragility (1). Low bone mineral density (BMD), measured by dual x-ray absorptiometry (DXA) has been shown to be associated with increased fracture frequency in children;(2) other factors, including vigorous activity are associated with changes in bone microarchitecture (3)(2)(4). Early identification and treatment of children who are at increased risk of fracture may lead to the optimisation of bone health in later life (4).

Current challenges to investigating bone fragility in children

There are limited technologies used to investigate childhood bone health. Bone biopsy is limited due to its invasiveness, pain and general anaesthetic requirements. Most commonly, BMD is measured by DXA. A low BMD in children is defined as a Z-score of less than or equal to -2.0 (5). The site-specific Z-score uses a reference population of children who are age, sex and ethnicity-matched. T-scores (adults) are not appropriate for children as they use the average peak BMD attained in early adulthood.

The clinical relevance of a low BMD in childhood is not fully understood (2). However, it is accepted that children with a low BMD are at an increased risk of developing osteoporosis. The International Society of Clinical Densitometry (ISCD) in 2014 stated that in children, *"…the diagnosis of osteoporosis requires the presence of both a clinically significant fracture history and low BMD"* (6). A significant fracture history is defined by either: - one or more vertebral crush fractures, two or more long bone fractures by the age of 10 years or three or more long bone fractures by the age of 19 years (6).

DXA calculates areal BMD (aBMD) by dividing the bone mineral content (BMC) by the bone area (BA). Hence, the depth of bones is not taken into account. This means that larger bones may be measured as having a falsely elevated aBMD. In other words, DXA is influenced by the size of the patient. This confounds the interpretation of aBMD in children (7). Furthermore, DXA does not allow independent assessment of cortical and trabecular bone (8).

HR-pQCT

High-resolution peripheral quantitative computed tomography (HR-pQCT) provides a direct assessment of bone microarchitecture and a true volumetric BMD (9). Similar to conventional CT, it uses x-rays from a rotating gantry. HR-pQCT images have a resolution of 82µm (Figure 1), the maximum scan distance is limited to 15cm and only peripheral sites (wrist and ankle) can be imaged. The scan takes under 3 minutes during which the patient must stay still. As a result, published research in children (8) is limited to those above 8 years old.

Currently, HR-pQCT is mainly used for research purposes, with there being only four scanners in the UK. Trabecular and cortical thickness can be assessed. Several measurements equating to bone histomorphometric estimates are also available, all with equal or less radiation dose

than DXA. Mathematical models are used to calculate a number of the outcome measures as well as direct measurements.

HR-pQCT has a very low ionising radiation dose (3μSv per scan), which is comparable to DXA (1-6μSv). Radiation is particularly important in children likely to have serial imaging. It is vital that the growth plates are not irradiated (9). To ensure this, an extremely low dose "scout" view of the joint is taken that allows identification of the region of interest (ROI); the ROI begins 1mm away from the epiphyseal growth plate in the same direction as the scan (Figure 2). The low radiation makes HR-pQCT attractive for use in children, particularly given its advanced imaging capabilities, likened to a " non-invasive biopsy"(8). From the HR-pQCT images, a number of engineering parameters related to stress and strain, can be derived through the creation of mathematical models in a process known as finite element analysis (Figure 3).

Limitations of HR-pQCT

A drawback of HR-pQCT is movement artefact, which is common when imaging the radius and tends to affect microarchitecture rather than density outputs (10). To achieve a high quality images, the limb must be securely fixed in a carbon fibre cast and the patient needs to have clear explanations to remain still. The site of the ROI alters over time due to growth and it may be difficult to compare results taken at different times. Future research may eliminate this issue. However, this is a universal challenge for any scanning modality used for longitudinal measurements in children.

The scanners operate close to the upper limits of their resolution capability. Microstructural and biomechanical measures (which depend on image resolution) have poorer precision when compared to density measurements (7). On the other hand HR-pQCT provides enhanced fracture prediction in comparison to lower resolution alternatives which may underestimate mechanical strength (10).

Clinically, accuracy errors may occur when HR-pQCT is used to scan children who have diseases that affect bone microarchitecture such as adolescent anorexia nervosa. In such conditions, cortical thinning makes it difficult to clearly differentiate the border between cortical and trabecular bone (12). Clearly this issue needs to be overcome, since it is likely to be in these very conditions that a precise understanding of the microarchitecture is required.

Conclusion

In summary, although HR-pQCT provides assessment of bone microarchitecture and estimated strength, there is still much we do not know with regards to its utility in the growing skeleton. This is especially true regarding the relationship between bone structure and strength in childhood and propensity to fractures later in life, although evidence for such a relationship is emerging (12)(13). HR-pQCT has the potential for inclusion in routine clinical practice to assist clinicians caring for children with metabolic bone disorders, but for now, in children, it remains a research tool.

References

1. Clark EM, Ness AR, Tobias JH. Bone fragility contributes to the risk of fracture in children, even after moderate and severe trauma. J Bone Miner Res. 2008;23(2):173–9.

2. Clark EM, Tobias JH, Ness a R. Association between bone density and fractures in children: a systematic review and meta-analysis. Pediatrics. 2006;117(2):e291–7.

3. Clark, EM Ness, AR Tobias J. Vigorous physical activity increases fracture risk in children irrespective of bone mass: a prospective study of the independent risk factors for fractures in healthy children. J Bone Min Res. 2008;7(23):1012–22.

4. Farr JN, Amin S, Melton LJ, Kirmani S, McCready LK, Atkinson EJ, et al. Bone strength and structural deficits in children and adolescents with a distal forearm fracture resulting from mild trauma. J Bone Min Res. 2014;29(3):590–9.

5. Wang Q, Cheng S, Alén M, Seeman E. Bone's structural diversity in adult females is established before puberty. J Clin Endocrinol Metab. 2009;94(5):1555–61.

6. Bishop N, Arundel P, Clark E, Dimitri P, Farr J, Jones G, et al. Fracture prediction and the definition of osteoporosis in children and adolescents: The ISCD 2013 pediatric official positions. J Clin Densitom. Elsevier Ltd; 2014;17:275–80.

7. Kirmani S, Christen D, van Lenthe GH, Fischer PR, Bouxsein ML, McCready LK, et al. Bone structure at the distal radius during adolescent growth. J Bone Miner Res. 2009;24(6):1033–42.

8. MacNeil J a, Boyd SK. Load distribution and the predictive power of morphological indices in the distal radius and tibia by high resolution peripheral quantitative computed tomography. Bone. 2007;41(1):129–37.

9. Paggiosi M a, Eastell R, Walsh JS. Precision of high-resolution peripheral quantitative computed tomography measurement variables: influence of gender, examination site, and age. Calcif Tissue Int. 2014;94(2):191–201.

10. Pistoia W, van Rietbergen B, Laib a, Rüegsegger P. High-resolution three-dimensional-pQCT images can be an adequate basis for in-vivo microFE analysis of bone. J Biomech Eng. 2001;123(2):176–83.

11. Faje AT, Karim L, Taylor A, Lee H, Miller KK, Mendes N, et al. Adolescent girls with anorexia nervosa have impaired cortical and trabecular microarchitecture and lower estimated bone strength at the distal radius. J Clin Endocrinol Metab. 2013;5(98):1923–9.

12. Farr J, Kholsla S, Achenbach SJ, Atkinson E, Kirmani S, MaCready L, et al. Diminished bone strength is observed in adult women and men who sustained a mild trauma distal forearm fracture during childhood. J Bone Min Res. 2014;10(29):2193–202.

13. Burrows M, Liu D, McKay H. High-resolution peripheral QCT imaging of bone micro-structure in adolescents. Osteoporos Int. 2009;21(3):515–20.