Strength and strain distributions obtained from digital wrist tomosynthesis (DWT) discriminate patients with and without a history of fragility fracture independently from BMD and stiffness

Ram N. Yadav[1], Daniel Oravec[1], Sudhaker D. Rao[2],Yener N. Yeni[1,3]

[1]Bone and Joint Center, [2]Division of Endocrinology, Diabetes and Bone & Mineral Disorders, Henry Ford Health, Detroit, MI, USA, [3]Henry Ford Health + Michigan State University Health Sciences, Detroit, MI, USA

ryadav1@hfhs.org

DISCLOSURES: Ram N. Yadav (N), Daniel Oravec (N), Sudhaker D. Rao (N), Yener N. Yeni (N)

INTRODUCTION: Osteoporosis is associated with reduced bone mineral density (BMD) and degraded bone microstructure, which lead to bone fracture under normal activity. Effective therapies exist to prevent bone fracture, but BMD from dual energy x-ray absorptiometry (DXA) fails to fully identify those at risk of fracture. With the advancement of *in vivo* high resolution peripheral QCT (HR-pQCT) imaging bundled with finite element analysis, the accuracy of bone fracture prediction has improved. However, due to the limited availability of HR-pQCT, these techniques have not come into mainstream use. Because of their wide availability in the mammography setting, bone screening using a digital breast tomosynthesis (DBT) scanner at the time of breast screening has been proposed as a viable solution [1]. Earlier studies have shown that BMD, microstructure and stiffness of the distal radius bone can be calculated using a digital tomosynthesis image of the wrist (DWT), and DWT derived stiffness discriminates fracture cases from non-fracture when BMD is not discriminative. However, the significance of stiffness was marginal for some models and its discriminatory ability was modest in previous studies [2]. Failure force and distribution properties of strains from the DWT based finite element model have the potential to enhance the utility of DWT; however, these were not examined previously. Therefore, the aim of this study was to examine the ability of DWT to discriminate patients with and without fragility fracture using DWT-FE derived failure force and strain distribution parameters in an *in vivo* pilot study.

METHODS: Under IRB approval, 21 women with history of at least one fragility fracture (Fx) (vertebral:5, forearm:15, hip:3, tibia:3) and 63 non-fracture (NFx) controls (Fx: age 57-78 years, NFx: age 52-88 years) were recruited. DXA based BMD was measured for femoral neck, total hip and lumbar spine to determine the osteoporosis status of each participant. In addition, vertebral fracture assessment was performed on lateral DXA images to identify unreported vertebral fractures. Subsequently, the nondominant arm (dominant if nondominant had history of fracture) of each participant was DWT scanned using a DBT scanner (GE Senographe Essential). Nine projection images of the forearm were taken over 25^o at 35 Kv and 50 mAs and reconstructed at 0.1 x 0.1 mm pixel size in frontal plane with 1 mm slice thickness. From the DWT image, the ultra-distal region, 15 mm in length, was extracted proximal to a 10 mm offset from the ulnar styloid process [1]. The extracted region was binarized using adaptive mean thresholding (Bruker CT-Analyser) and a voxel based finite element mesh was generated for each participant. Compressive loading was simulated along the proximal distal direction in linear models once using homogeneous (BIN-FE) and once using gray value-based material (GV-FE) properties. Stiffness (K) and distribution properties (average, standard deviation) of von Mises, tensile and compressive principal strains were calculated. Failure strength (F) was also calculated as the load at which 2% of total number of elements reached 0.007 strain [3]. Fx and NFx groups were compared using t-tests or Wilcoxon tests based on normality. Generalized linear models (GLM) framework was used to examine multiple variables and construct logistic regression models. Area under the receiver operating characteristic curve (AUC) was recorded from each model as a measure of the model's discriminative ability. All analyses were carried out in R with significance set as $p<0.05$.

RESULT: The differences in age ($p>0.2$) and minimum T-score ($p>0.9$) were not significant between Fx and NFx groups. Stiffness and failure strength from BIN-FE and GV-FE were lower whereas standard deviation of tensile principal strains ($\varepsilon_{T.SD}$) was higher in the Fx than in the NFx group (Table 1), while other strain variables had no significant difference. GLM results indicated that these variables are significant predictors of Fx status (Table 1). $\varepsilon_{T.SD}$ was the most discriminatory variable for fracture status (AUC=0.74, Fig 1(A)), and multiple regression models indicated that it was significant ($p<0.02$) independently from stiffness ($p<0.3$). For the Fx group, most elements have either high or low ε_T and a few elements have mid-values of ε_T, whereas the NFx group have more mid and less extreme values (Fig 1(B)).

DISCUSSION: The lower values of failure force and stiffness for Fx group, despite similar T-scores, confirms that DWT-FE has capability to detect attributes of at-risk bones independently from BMD. As in previous work [2], stiffness was marginally significant for homogenous models in this larger sample. In contrast, failure force and strain heterogeneity were significant for both model types and more discriminative of fracture. Furthermore, the ability of $\varepsilon_{T.SD}$ to separate Fx and NFx groups was considerably higher than, and independent from, K and F. These results support utilization of image-based FE models beyond calculation of bulk elastic properties, and suggest that parameters of local deformation behavior and strength as measured by DWT-FE can improve fracture risk assessment. The explanatory capability of higher $\varepsilon_{T.SD}$ for fracture is consistent with lower tensile than compressive failure strain of bone and that a majority of elements undergo tensile failure in cancellous bone [4]. Our results suggest that structural differences in cortical-trabecular junctions in the distal radius play a role in strain distributions. Future work is needed to elaborate the underlying mechanism.

CLINICAL RELEVANCE: This study demonstrated that DWT-FE has capability to capture bulk as well as local biomechanical properties, which can discriminate participants with fracture from those without. As such, these results suggest that the accuracy of fracture risk screening can be improved in the highly accessible environment of mammographic imaging.

REFERENCES: [1] Yeni et al., 2021, Bone, 144:115804. [2] Yadav et al., 2023, Bone, 177:116901. [3] Pistoia et al., 2002, Bone, 6: 842–848. [4] Bevil et al., 2009, Journal of Biomechanics 42: 2165–2170

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Table 1: Descriptive data of FE output of Fx and NFx group along with area under the curve of receiver operating curve

Variable	Fx (Mean±SD)	NFx (Mean±SD)	AUC
K_{BIN} (kN/mm)	24.4±2.3	25.8±3.6*	0.61*
K_{GV} (kN/mm)	26.9±3.9	29.7±6.2**	0.64**
F_{BIN} (kN)	0.604±0.157	0.691±0.169**	0.67**
F_{GV} (kN)	0.533±0.153	0.653±0.231**	0.65**
$(\varepsilon_{T.SD})_{BIN}$	0.0092±0.0003	0.0090±0.0003***	0.68***
$(\varepsilon_{T.SD})_{GV}$	0.0103±0.0005	0.0099±0.0005****	0.74****
p value : *<0.1, **<0.05,***<0.01,****<0.001			

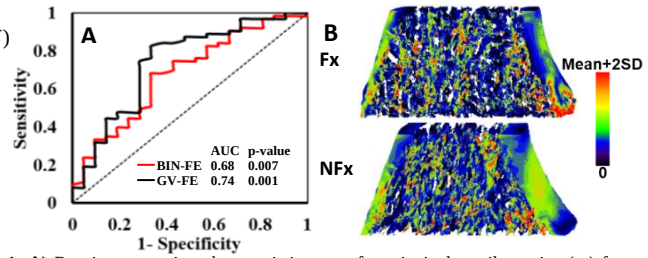

Fig 1: A) Receiver operating characteristic curve for principal tensile strains (ε_T) from BIN-FE and GV-FE models. B) Distribution of ε_T showing that highest strains are at the distal end in cortical bone for the Fx group whereas the values are low to medium at the same locations for the NFx group, yielding higher $\varepsilon_{T.SD}$ for the Fx group.