## E-Appendix

Any method that predicts fracture risk must be able to measure both changes in bone tissue material properties and changes in bone geometry induced by the neoplasm. The bone tissue modulus is a function of the bone mineral density[29,30]. The modulus of elasticity ($E$), which is the intrinsic stiffness of the bone (in MPa), for each pixel in the image was calculated from the apparent density with use of empirical relationships[29,30]. In order to use these density-to-modulus relationships, the bone mineral density measured with quantitative computed tomography was adjusted by the mass ash fraction ($f_{ash}$) to convert bone mineral density to apparent bone density ($\rho_{app}$) in g/cm$^2$, which represents the density of the combined mineral and organic phases of bone:

$$\rho_{app} = \frac{\rho_{ash}}{f_{ash}} \quad \text{(Equation A1)}$$

where $f_{ash} = 0.66$[34]. A minimum apparent density of 0.05 g/cm$^2$ was used as a threshold to separate bone from soft tissue. For trabecular bone, a power law relationship[29] was used:

$$E = 0.82(\rho_{app}^2) + 0.07; \quad \text{(Equation A2)}$$

For cortical bone a linear relationship[30] was used:

$$E = 21.91(\rho_{app}) - 23.5. \quad \text{(Equation A3)}$$

The transition from trabecular to cortical bone was set at the point where the two equations intersect at 1.123 g/cm$^2$. The shear modulus ($G$), in MPa, for transverse cross sections through the bone perpendicular to the primary trabecular orientation was calculated from the modulus of elasticity[47]:

$$G = \frac{E}{2.6}. \quad \text{(Equation A4)}$$

Bone geometry is represented by the cross-sectional area and moment of inertia[31]. The moment of inertia describes analytically how the bone mass is distributed in space relative to a bending axis. It varies as the fourth power of the distance of the bone tissue relative to a specific bending axis. It is a vector; therefore, it has both a magnitude and a direction. The principal moments of inertia describe the magnitude and direction of the (mutually orthogonal) maximum and minimum moments of inertia for a cross section through the bone. The maximum moment of inertia corresponds to the bending axis through the bone cross section *most* resistant to bending deformation, while the minimum moment of inertia corresponds to the bending axis through the bone cross section *least* resistant to bending deformation. As an example of this principle, consider the bending of a yardstick: although the mass of the yardstick is constant, it is much easier to bend the yardstick when the bending axis is oriented along its thickness (minimum principal moment of inertia) than it is to bend the yardstick when the bending axis is oriented along its width (maximum principal moment of inertia).

Rigidity, the product of the bone tissue modulus of elasticity and bone cross-sectional geometry, describes the structural behavior of a bone and its resistance to deformation when subjected to axial, bending, or twisting loads[28]. The axial rigidity *(EA)*, bending rigidity *(EI)*, and torsional rigidity *(GJ)* for each transaxial cross-sectional image were calculated by summing the modulus-weighted area of *each* pixel of the bone section by its position relative to the centroid of the bone (Fig. 2):

$$EA = \sum_{i=1}^{N} E_i da \quad \text{(Equation A5)}$$

$$EI_x = \sum_{i=1}^{N} E_i y'^2_i \, da \qquad \text{(Equation A6)}$$

$$GJ = \sum_{i=1}^{N} G_i \left( x'^2_i + y'^2_i \right) da \quad \text{(Equation A7)}$$

where $E_i$ is the modulus of elasticity, which is a function of the apparent bone density ($\rho_{app}$) at each pixel ($i$); $da$ is the pixel area; $N$ is the total number of pixels forming the image; $G_i$ is the shear modulus, which is a function of the modulus of elasticity ($E_i$) at each pixel ($i$); $x'_i$ and $y'_i$ are the horizontal and vertical distances of each pixel from the modulus weighted centroid $(\bar{x}, \bar{y})$ of the bone on the cross section calculated as:

$$\bar{x} = \frac{\sum_{i}^{N} x_i E_i da}{\sum_{i=1}^{N} da}, \bar{y} = \frac{\sum_{i}^{N} y_i E_i da}{\sum_{i=1}^{N} da}. \quad \text{(Equation A8)}$$

where $x_i$ and $y_i$ are the horizontal and vertical coordinates of each pixel relative to the origin of the cross section. $A$ is the total cross-sectional area of bone, $I_x$ is the moment of inertia taken about the horizontal ($x$) bending axis in the transverse plane, and $J$ is the polar moment of inertia.