Purpose/Objective: More than half of cancer patients receive radiotherapy for radical or palliative purposes. Increasing survival rates in cancer patients make it important to study late side-effects, including secondary radiation-induced cancers. Although a number of predictive models exist, the absolute accuracy of these models in the radiotherapy dose range is limited partly due to scarcity of data and partly by extrapolation beyond historical data bounds. One of the challenges faced with applying models to the highly spatially varying dose distributions produced in modern radiotherapy is dose heterogeneity within organs of interest. The aim of this work is to investigate the difference between using mean dose (MD) and high-resolution voxel-by-voxel dose (VbV) maps for calculating malignant induction probability (MIP).

Materials & Methods: A 3D conformal radiotherapy (3DCRT) and actively scanned proton plans were used for an adult patient and a teenage patient with medulloblastoma. MIP is calculated for each patient using the linear-quadratic (LQ), linear (LIN) and linear-no-threshold (LNT) models with in-house developed code. MIPs calculated using the mean dose to the organs as well as voxel-by-voxel dose are compared for individual organs and the whole body. A 3DCRT plan and an actively scanned proton therapy plan for an adult female MB patient were supplied by collaborators at Mayo Clinic. The prescribed dose was 36 Gy to the whole brain and spine with a 19.8 Gy boost to the posterior fossa (1.8Gy/fx).

All calculations are performed with a predefined priority list used to determine which structure each voxel is assigned to (and therefore which set of model parameters to apply). For VbV, the MIP was calculated using high-resolution dose maps that utilizes doses for each voxel, and for the mean dose, the mean dose of the whole organ was used to calculate MIP.

Materials & Methods: The linear association, secondary cancer risk. This should be taken in consideration when designing studies of secondary cancer risk (f).

Results: Demonstrate large systematic differences between the risk estimates produced using either mean dose or voxel-by-voxel calculation. Although the relative relation between \text{MIP}_{\text{VbV}} and \text{MIP}_{\text{MD}} remains broadly constant, using mean dose in heterogeneous dose distributions potentially overestimates MIP and, by association, secondary cancer risk. This should be taken in consideration when designing studies of secondary cancer risk (f).

Conclusions: Results demonstrate large systematic differences between the risk estimates produced using either mean dose or voxel-by-voxel calculation. Although the relative relation between \text{MIP}_{\text{VbV}} and \text{MIP}_{\text{MD}} remains broadly constant, using mean dose in heterogeneous dose distributions potentially overestimates MIP and, by association, secondary cancer risk. This should be taken in consideration when designing studies of secondary cancer risk (f).

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MIP Models used: The linear-quadratic malignant induction model (LQ): \text{MIP} = \mu (y + 5d^2) e^{-\alpha (y + 5d^2)}. The linear malignant induction model (LIN): \text{MIP} = \mu D e^{-c(y + 5d^2)}, Linear-no-threshold malignancy induction model (LNT): \text{MIP} = \mu D. Linear-with-threshold malignancy induction model. \text{SF}: the surviving fraction of cells given in (n) fractions of dose (d), \alpha and \beta: the radiosensitivity parameters, are the linear and quadratic component of the curve, respectively. y and \delta: the malignant induction coefficients. \mu: linear coefficient, D is the total dose.