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A Fully Automated Pipeline for Vertebral Structural Assessment From Medical Images. Application Under Metastatic Conditions

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ABSTRACT

Spinal bone metastases often lead to vertebral fractures and other skeletal events that severely affect patients' quality of life. Predicting structural failure is essential for guiding treatment and preventing complications. However, conventional assessment tools have limited predictive power, highlighting the need for computational methods capable of simulating disease progression and its mechanical consequences. This study aimed to develop a fully automated, patient-specific methodology to predict vertebral structural behavior from computed tomography (CT) data, supporting clinical decision-making and treatment planning. The proposed pipeline integrates three main components: a deep neural network for semantic segmentation of vertebrae and metastatic regions from CT scans, the Coherent Point Drift (CPD) algorithm to ensure consistent alignment and automated definition of boundary conditions across datasets, and the Cartesian Grid Finite Element Method (cgFEM) to simulate the vertebral mechanical response under metastatic involvement. Model performance was evaluated by comparing the predicted outcomes with reference data, using precision, sensitivity, and specificity to assess reliability. The proposed workflow achieved full automation from CT imaging to fracture risk estimation. The segmentation module showed high accuracy across multiple metrics, enabling robust model generation. Geometric normalization and CPD-based boundary condition assignment standardized vertebral geometries across studies, while cgFEM simulations provided clinically interpretable metrics such as safety factors and stability variations associated with tumor size, location, and density. These analyses enabled the identification of scenarios linked to a higher fracture risk. The main limitations include the use of fixed boundary conditions and a predefined voxel threshold, which may reduce physiological realism and generate false positives. Overall, this work presents an end-to-end, patient-specific framework for automated fracture risk evaluation in metastatic vertebrae. By combining deep-learning-based segmentation, geometric normalization, CPD alignment, and cgFEM simulations, the method produces clinically relevant outputs that can guide therapeutic strategies. Future developments will focus on integrating patient-specific loading data and predictive modeling to support incorporation into clinical decision support systems.

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1 | Introduction

Spinal metastasis is a common condition in cancer patients, potentially developing in 30%–50% of cancer cases [1], depending on the cancer type. Post-mortem studies have shown that the prevalence of spinal metastases is particularly high in patients with breast and prostate cancer, reaching up to 90% and 70%, respectively [2]. This condition can cause serious complications, such as intense pain, requiring high doses of opioid analgesics, possible structural collapse of the vertebra, hypercalcemia, spinal cord compression due to epidural space invasion, and the appearance of other Skeletal Related Events (SRE), which can significantly diminish the patient's quality of life.

In this context, spinal bone metastases may manifest as lytic or blastic lesions. Lytic lesions are the most common type in bone metastasis and are characterized by a reduction in bone density in the affected area, resulting in a loss of its mechanical properties and, consequently, its load-bearing capacity, potentially leading to structural failure. Since this type of lesion involves direct destruction of bone tissue without complex alterations in load distribution, its failure mechanism is usually simpler compared to blastic lesions. On the other hand, blastic lesions are characterized by increased bone density and consequent stiffness in the affected area, which may lead to vertebral failure through a process called “Stress Shielding” [3, 4]. In this type of failure, the stiffening of the affected bone area causes a redistribution of loads in the bone, which tend to pass through the stiffer area, the tumor, thereby unloading the surrounding area. As a result, this surrounding region tends to reabsorb and, eventually, like in the previous case, to suffer structural collapse. Both types of lesions pose a risk to the structural stability of the affected vertebra, consequently endangering the spinal cord.

Currently, the treatment of bone metastasis remains a challenge. Existing options include surgery, which would be used in situations with favorable prognostic factors of the tumor, according to the malignancy grade and the presence of visceral and bone metastases; radiotherapy, which, if used timely, can eliminate the need for surgical intervention in radiosensitive tumors [5]; and finally, the use of chemotherapeutic agents such as bisphosphonates, which suppress bone resorption and can delay the onset of bone lesions [5]. Selecting the most appropriate treatment for each patient is essential, as it determines the course of the condition and the patient's quality of life. To properly select the optimal treatment, tools that allow for the prediction of structural collapse risk in metastasis-affected vertebrae are needed. The literature contains publications in which structural analysis of metastatic vertebrae is performed through laborious manual processes [6, 7]. However, to the author's knowledge, there are no personalized analysis tools of this kind with a sufficient level of automation and processing speed to allow their application in demanding clinical environments.

Among the tools developed in recent decades for personalized patient analysis, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) stand out. Both technologies enable 3D recording of patient spines and detailed representation of the vertebral body, potentially including tissues, ligaments, and intervertebral discs in the case of MRI [8]. Although CT scans are the most commonly used technique for tumor evaluation,

they have limitations in distinguishing between lytic and blastic lesions and may fail to clearly represent lesions causing small structural changes, complicating clinical decision-making in such scenarios [9]. Both technologies allow graphical identification of metastatic lesions; however, mere graphical identification does not quantify the structural quality of the affected vertebrae.

The limitations of solely graphical information obtained through medical imaging techniques have led to the development of post-processing procedures for this graphical data. Their goal is to create patient-specific mathematical models that, incorporating additional information, such as the physics of structural behavior of the material, represent the structural and anatomical characteristics of the vertebrae shown in the image, thus enabling computational simulations of their behavior [10]. Generating these models allows for simulation of various structural behavior scenarios based on the patient's medical image, from predicting metastasis progression in the bone to evaluating the impact of a performed surgery [11]. However, creating these models can be complex, as it requires a pre-segmented medical image of the vertebrae to be analyzed, which, due to the complexity of medical images, must be done by a specialized physician [12].

A possible classification of medical image segmentation techniques divides them into two main branches: segmentation based on traditional methods and segmentation using artificial intelligence applications. Traditional segmentation methods focus on semi-automatic or manual algorithms that segment according to manually entered parameters, including contour-based, region-based, and texture-based techniques. These methods suffer from undersegmentation and oversegmentation issues and are highly dependent on choosing the right parameters for the image [13], in addition to the obvious time cost for medical specialists, which is their main drawback.

On the other hand, AI-based segmentation has seen a boom in recent years. These techniques rely on neural networks for segmentation. Their main features include full or near-full automation of the process and high accuracy in medical image segmentation [14]. Among the most recognized machine learning methods are Convolutional Neural Networks (CNNs) [15], which are highly capable of learning complex and hierarchical image features but are prone to overfitting without proper parameter tuning; U-Nets [16], specifically designed for medical image segmentation, which may perform less effectively on large datasets compared to other architectures; and Mask R-CNNs [17], capable of segmenting each individual object instance in an image with high precision but featuring high architectural complexity, which may complicate their implementation and tuning. Since each of these techniques has advantages and drawbacks, the literature also features combinations of these approaches to achieve synergistic effects [18, 19].

Creating structural simulation models from medical images requires computational mechanics techniques, typically the Finite Element Method (FEM), widely used in industrial environments. However, applying FEM in clinical practice poses several challenges, such as the need for substantial computational resources, generating a CAD model of the organ to be analyzed (in this case, vertebrae) to obtain accurate results, and the time required from both clinical and structural analysis specialists

for segmentation and model generation [20]. One solution to mitigate these issues involves techniques based on finite element meshes not conforming to geometry, using voxel-associated values to represent the image and assign properties to each element in the finite element mesh. One such technique is the Cartesian Grid Finite Element Method (cgFEM) [21, 22], which is based on Cartesian meshes and can use h-adaptive meshes to improve model precision [22–24].

cgFEM enables the creation of patient-specific models from pre-segmented medical images without requiring a CAD model of the patient's vertebra, which would be necessary with standard FEM. This facilitates structural behavior analysis of segmented vertebrae and prediction of collapse risk. Once vertebral models to be analyzed are obtained, it is necessary to specify the boundary conditions (displacement restrictions and loads) also in a personalized manner to perform structural analysis.

Thus, there are currently procedures that allow for personalized estimation of fracture risk in metastasis-affected vertebrae. However, several processes remain non-automated and must be manually performed by expert personnel. The cost, evaluated in expert work-hours, associated with these processes means that, in their current development state, these technologies are not applicable in demanding clinical settings.

This study proposes a fully automated methodology to predict, in a personalized way, the risk of structural failure in metastasis-affected vertebrae based on the patient's CT image. The proposed methodology includes a set of techniques to carry out structural assessment of the vertebrae based on the patient's CT image. Thus, it employs a Deep Learning technique for semantic segmentation of each vertebra in the spine, the application of the Coherent Point Drift (CPD) algorithm, which enables applying boundary conditions on each vertebra by transferring pre-defined conditions from reference vertebrae, thus automating their definition [25, 26], and finally, the use of cgFEM for structural finite element analysis of the vertebrae.

Taking this into account, the paper will be divided into the following sections. Section 2 will present a general overview of the methodology and the different steps taken in its development; Section 3 will describe the validation of the methodology and its individual components; Section 4 will provide an example of the analysis of a segmented vertebra, based on established indicators; and finally, the project discussion and conclusions will be presented in Sections 5 and 6.

2 | Methodology

The proposed methodology for the personalized structural analysis of tumor-affected vertebrae is divided into two stages: an offline stage, focused on the spinal segmentation process and CPD base definition, and an online stage, centered on the structural analysis of the vertebrae. The workflow of each of these stages is shown, respectively, in the Figure 1.

As shown in Figure 1, the workflow of the offline stage is divided into two phases. The Deep Learning model training phase consists of the following steps: the first involves acquiring a dataset

composed of medical images from healthy patients (CT scans), along with the mask for each vertebra, enabling their segmentation. This dataset is used to train a Deep Learning model, whose function is to generate a semantic segmentation model of the spine that automatically identifies the patient's vertebrae and returns them individually cropped from the original CT scan. This process is described in more detail in Section 2.1.1.

On the other hand, due to the difficulty of automatically defining BCs (boundary conditions) on vertebrae with singular geometries, the second offline phase focuses on defining the reference geometries for applying CPD. In this case, it consists of creating a set of reference vertebrae with boundary conditions manually established. This procedure for creating the vertebrae is described in Section 2.1.2.

Finally, in the online stage, the segmentation model is applied to the CT scan of a new patient to obtain the segmented vertebrae of the spinal column. Subsequently, a normalization process is applied to each segmented vertebra (Section 2.2.1), in order to facilitate the automation of the application of BC and the structural analysis of each vertebra. The definition of BC is performed using CPD from the reference vertebrae established in the offline stage. Once the conditions are determined, a patient-specific FEM model is generated, enabling the evaluation of the structural behavior of the patient's vertebra as shown in the CT scan. Additionally, different tumor growth scenarios can be assessed using a parameterized tumor model, in order to observe its repercussions on the structural behavior.

As a final note, it is important to consider that this paper presents a methodology that utilizes a specific set of techniques (Machine Learning for semantic segmentation of vertebrae; CPD for boundary condition definition; and cgFEM for obtaining the structural behavior of vertebrae, taken from the following publication [27], in which cgFEM is used to generate a surrogate model of a vertebra to perform personalized structural analyses) with the ultimate goal of defining a fully automated procedure for the structural analysis of metastasis-affected vertebrae. Using standard patient data available in cancer patient treatments, this procedure aims to be compatible with the demanding requirements of clinical environments. The following subsections describe the techniques used and how they have been applied or adapted to achieve the intended objective.

2.1 | Offline Workflow

As previously mentioned, the offline block consists of two main stages: the construction and training of a Deep Learning model, and the generation of reference vertebrae under predefined boundary conditions. This section describes in detail the procedures corresponding to each of these stages.

2.1.1 | Offline Workflow: Deep Learning Model Training

The first stage of the offline block consists of training a Deep Learning model using a medical image dataset to enable automatic semantic segmentation of patient vertebrae. The vertebrae

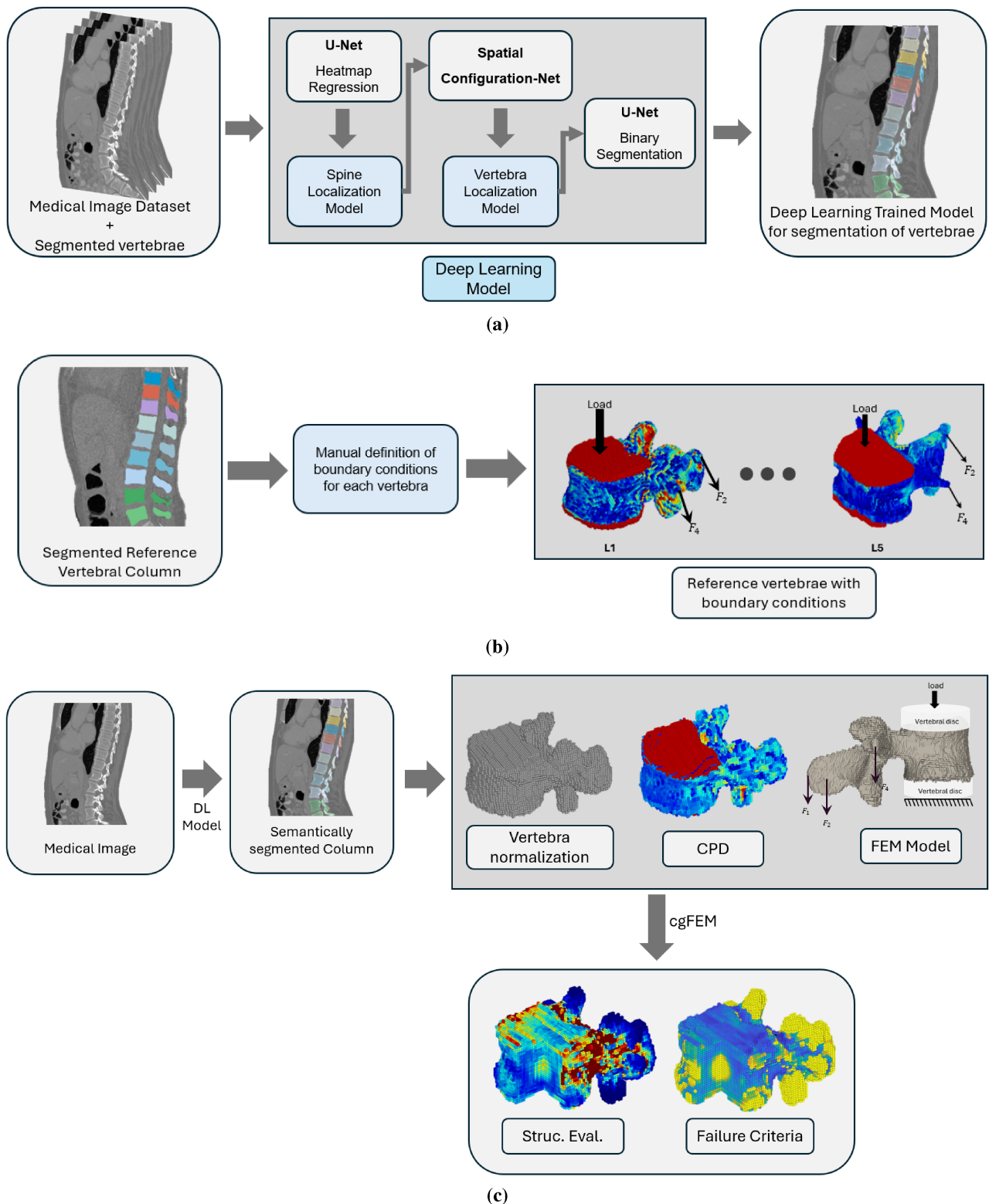


FIGURE 1 | Workflows employed in the development of the proposed methodology. (a) Offline workflow for deep learning model training. (b) Offline workflow for the generation of boundary conditions for the reference vertebrae. (c) Online workflow.

dataset, along with the mask data used for segmentation training, was extracted from the Verse 2020 challenge “Verse: Large Scale Vertebrae Segmentation Challenge” [28, 29]. This challenge’s main objective is to develop automated algorithms for identifying and segmenting vertebrae. Unlike the 2019 dataset version [30],

the 2020 version includes a greater number of medical images, retains data from previous versions, and introduces atypical spinal conditions (L6, T13) for algorithm training. The selected segmentation code is the one that achieved the highest segmentation accuracy, as presented by Payer et al. (2020) [19]. This

reference proposes a progressive refinement approach divided into three blocks: spine localization within the medical image, vertebra identification and localization, and finally, vertebra segmentation, all of which employ convolutional neural networks (CNNs) trained for each phase. The selected CNNs are tailored to the specific goals of each phase to achieve optimal segmentation.

The first block for semantic segmentation is trained with a model for spine localization that produces a heatmap of the approximate coordinates of the vertebrae, facilitating their subsequent localization. The neural network has the following characteristics:

- A variant of U-Net [31], adapted to perform average pooling instead of max pooling and linear upsampling instead of transposed convolutions.
- Input: Resampled CT scans at a resolution of $[64 \times 64 \times 128]$.
- Output: Heatmap of the same size, indicating the probability of spine location.

The second block of semantic segmentation is trained with a vertebrae identification and localization model that provides the location of the center of mass of each vertebra, which is necessary for subsequent segmentation. The network used has the following features:

- SpatialConfiguration-Net (SC-Net) proposed by Payer et al. (2019) [32], combining local landmark appearance with spatial configuration and using a modified L2-loss.
- Detects various maxima in the heatmaps predicted by U-Net, allowing determination of the first and last vertebrae present in the image.
- Establishes rules for identifying the remaining vertebrae: consecutive vertebrae must not be closer than 12.5 mm or

farther than 50 mm; due to the descending prediction order, subsequent landmarks must not be higher than previous ones.

- Input: Resampled CT scans from the U-Net and corresponding heatmap outputs.
- Output: Final coordinates of the vertebrae's centers of mass in the CT scan.

Finally, the third semantic segmentation block is trained with a binary segmentation model that produces masks for each vertebra and its individual segmentation. Since this model's sole function is segmenting each vertebra from the medical images, it is applied individually to each vertebra. The network's characteristics are:

- U-Net [31] focused on binary segmentation, composed of a total of 23 convolutional layers.
- Crops the region around the vertebra to be segmented, placing its landmark at the center of the cropped image.
- Creates a Gaussian map around the cropped image.
- Input: Gaussian images and cropped vertebrae, both resampled to $[128 \times 128 \times 128]$.
- Output: Vertebrae masks and their segmentation from the original medical image.

To better understand the process, Figure 2 shows the segmentation workflow and its results, where U-Nets and SC-Net are trained offline using the machine learning dataset and masks.

Once the training of the different networks involved in the segmentation process is completed, a procedure is obtained that allows for the semantic segmentation of a spine medical image, producing the segmented image of each individual vertebra

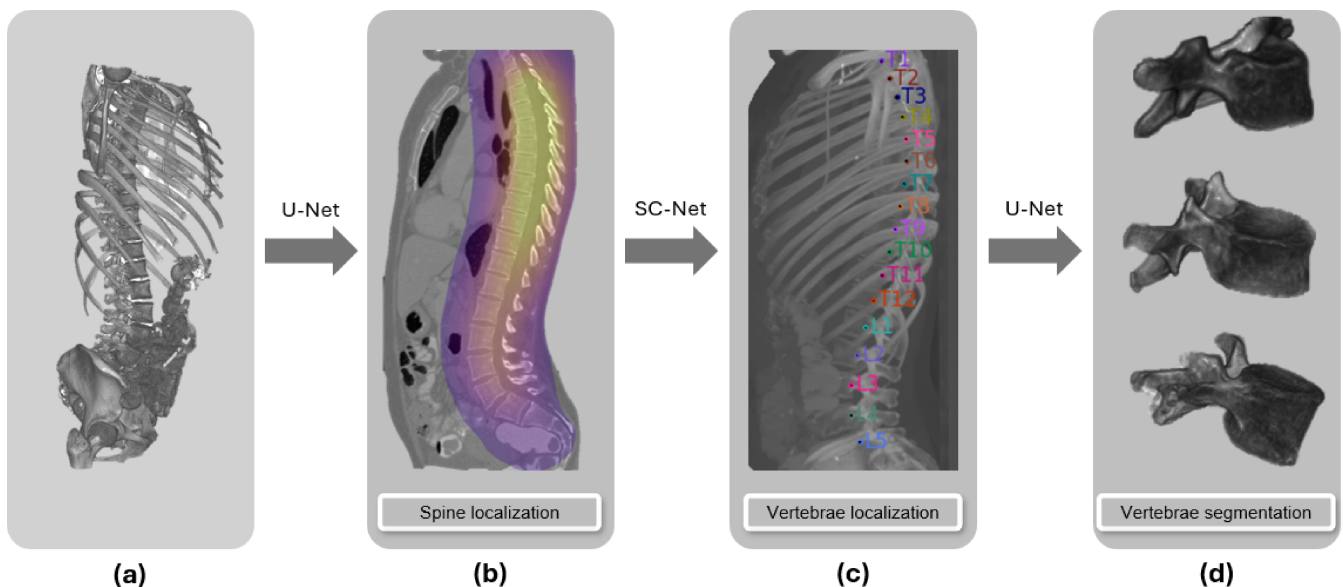


FIGURE 2 | Semantic segmentation pipeline and corresponding results. (a) Original CT scan of a patient. (b) Output heatmap indicating the location of the spine, obtained from the trained spine localization model. (c) Output showing the locations and labels of the vertebrae, obtained from the trained vertebra localization model. (d) Output of the individually segmented vertebrae, extracted using the vertebra segmentation model.

for further manipulation and structural analysis using cgFEM. Additionally, Section 3.1 presents the visual and quantitative validation of the semantic segmentation, thereby supporting the proposed methodology.

2.1.2 | Offline Workflow: Reference Vertebrae Boundary Conditions Creation

As previously discussed, the application of personalized boundary conditions is performed through a projection procedure (CPD), which requires the prior definition of a set of reference vertebrae with manually established boundary conditions.

To this end, the first step in constructing the reference vertebrae is to apply the Deep Learning model to a healthy spine from the Verse2020 dataset, yielding segmented vertebrae that serve as the basis for creating the reference models. Subsequently, boundary conditions are defined according to the criteria in Ref. [27], which emphasizes the need to apply forces on the vertebra that emulate intervertebral disc function and several point loads at muscle insertion zones. However, since the structure of the intervertebral discs is not available for applying the corresponding forces, a procedure is defined to simulate discs on the upper and lower surfaces of the segmented vertebral body. This process automatically identifies these surfaces and then generates the simulated intervertebral tissue for force application. In this paper, the procedure is applied only to lumbar vertebrae, but it could also be extended to the rest of the spine.

Regarding the magnitude, direction, and placement of the loads, these are defined in Ref. [33], where a compressive load is applied to the upper intervertebral disc, perpendicular to the disc surface, and five point loads are placed on specific areas of the vertebral structure. These loads represent the action of different muscles and ligaments connecting the vertebra to the rest of the spine, with their directions and magnitude interpolated from the compressive load (see Table 1). In particular, F_1 represents the interspinous ligament, F_2 and F_3 correspond to the multifidus muscle, and forces F_4 and F_5 represent the quadratus muscle. A motion restriction is applied to the lower intervertebral disc. Figure 3 illustrates the boundary conditions applied to a vertebra for analysis.

It should be noted that the load placement process can be labor-intensive and must be performed by a clinical expert. However, it only needs to be done once per vertebra type, since the entire procedure is subsequently automated using CPD.

TABLE 1 | Applied loads on the vertebra and their normalized components with respect to the primary compressive load (in Newtons).

	F_1	F_2	F_3	F_4	F_5
$ F $	0.073	0.093	0.089	0.050	0.063
F_x	0	0	0	0	0
F_y	0	0.0465	-0.0445	0.0171	-0.0215
F_z	-0.073	0.0805	-0.0771	-0.0471	-0.0592

2.2 | Online Workflow

Once the Deep Learning model has been trained and the reference vertebrae have been defined, the online block of the proposed methodology is carried out. The online phase consists of the following stages:

- Application of the Deep Learning model to the spine with vertebrae to analyze
- Normalization of the vertebrae set
- Application of boundary conditions via CPD
- Finite element analysis with artificial tumor

However, it should be noted that once the vertebrae are segmented from the medical image, the rest of the process is applied individually to each vertebra.

2.2.1 | Online Workflow: Vertebra Segmentation and Normalization

The segmentation process is performed automatically by applying the Deep learning model, as previously mentioned, however due to the variety of orientations used in medical images to express the anatomical reference system, and the fact that these images do not share the same matrix size or voxel dimensions, it is necessary to apply normalization to the medical images of the vertebrae to facilitate their use in the analysis and full process automation.

The normalization process is divided into two parts: reorientation of the medical images and restructuring of their data. Reorientation is necessary because not all CT machines use the same anatomical reference system, potentially using systems like RAS (Right, Anterior, Superior) or LPS (Left, Posterior, Superior) [34]. This reorientation is automatically performed by a script that converts any medical image reference system to RAS, thereby standardizing the spine for easier automatic analysis.

Additionally, because vertebra segmentations are unique to each case, the bounding boxes of cropped vertebrae contain data matrices of different sizes, making structural analysis automation impossible. For this reason, an automated normalization process is implemented to restructure the data so that all cases share a constant voxel and matrix size, which facilitates full automation.

Overall, the process reorients the vertebra to the RAS reference system, resamples its voxel size to 1.058 mm in all directions, and resizes the matrix to $[128 \times 128 \times 128]$.

2.2.2 | Online Workflow: Coherent Point Drift and Boundary Conditions

For the application of boundary conditions, it is important to recognize that, unlike typical structural calculations in mechanical components, where the object is represented by a CAD model that facilitates boundary condition definition, here the vertebra is represented by voxels. Furthermore, each patient's vertebra has a

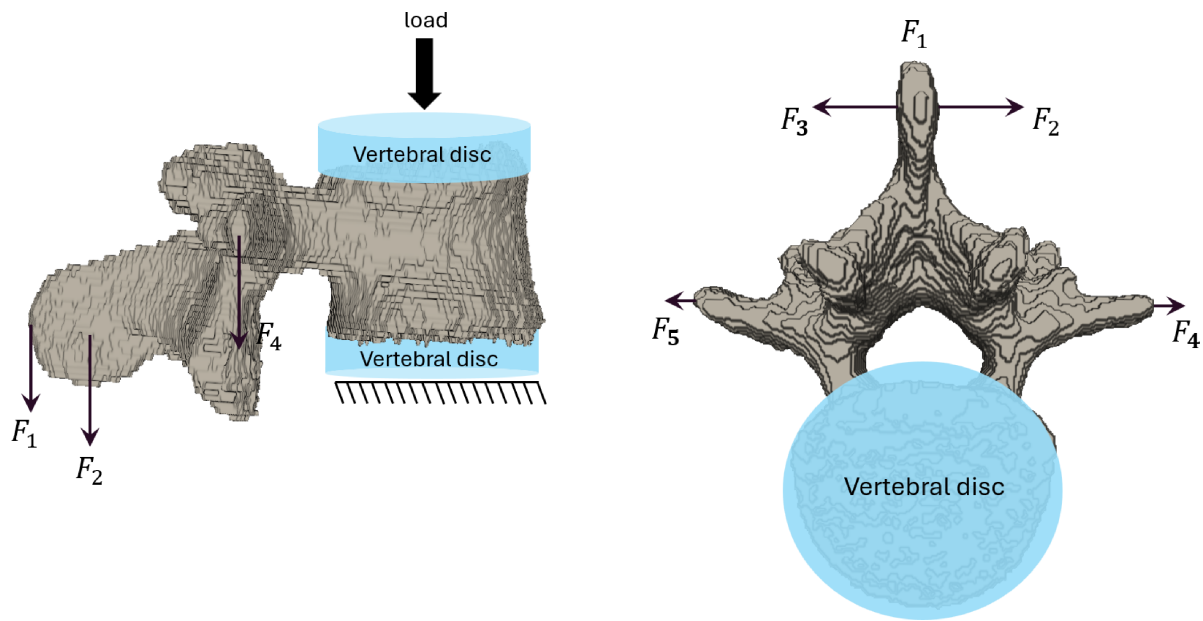


FIGURE 3 | Reference vertebra with all boundary conditions identified and both intervertebral discs in place.

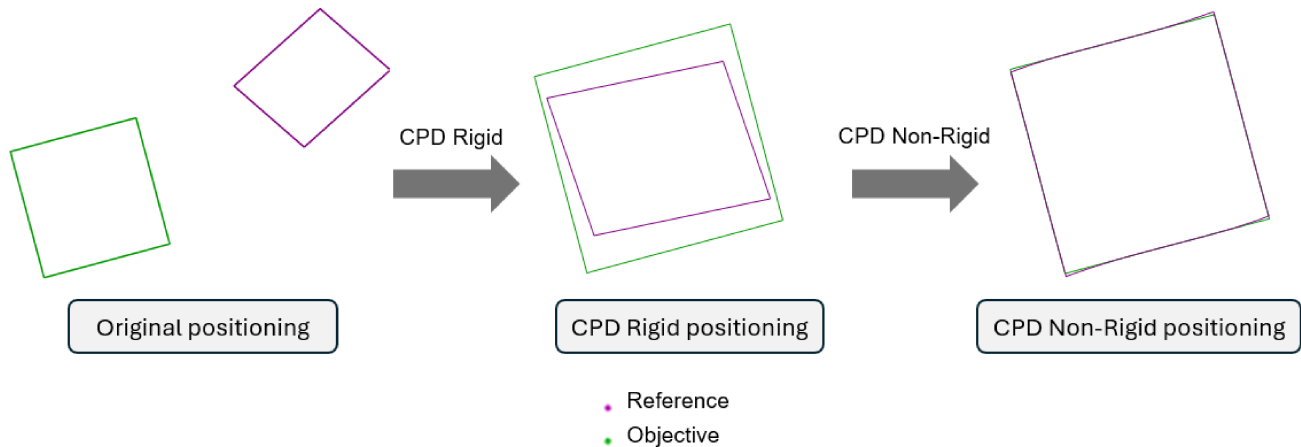


FIGURE 4 | Example of rigid and non-rigid Coherent Point Drift transformations for the registration of two point clouds. The geometries consist of two squares with different sizes, initial positions, and orientations.

unique geometry, meaning that the same BC cannot be uniformly applied, which challenges the goal of full automation. For this reason, the Coherent Point Drift (CPD) method is proposed.

CPD is an algorithm designed to register two point sets by treating the reference set as a sample from a probability distribution and assuming the input set is drawn from this distribution, searching for the optimal transformation that aligns the two. In our case, the point clouds of the vertebrae are generated from the voxels of the medical image, placing a point at the center of each voxel that defines the vertebral surface.

CPD uses an iterative approach based on the Expectation–Maximization (EM) algorithm [35], making it highly versatile and accurate. One of its main features is its ability to handle two types of transformations: rigid (including only rotations and translations, preserving the internal structure of the point set) and non-rigid (allowing local deformations, suitable for registering data with complex changes).

To generate geometry-adapted boundary conditions, the CPD application process is divided into several steps. First, the outer voxels of the vertebra to analyze are selected and a point is assigned to each, forming the point cloud required for CPD. Then, rigid CPD is applied between this point cloud and that of the corresponding reference vertebra (from the offline phase), aligning their position and orientation.

Lastly, non-rigid CPD is applied so that the reference vertebra adapts to the vertebra under analysis. This allows for identifying the regions on the patient's vertebra where the boundary conditions for the cgFEM analysis must be established.

For better understanding, Figure 4 shows an example of both rigid and non-rigid transformations applied to squares to illustrate the CPD transformations.

Thus, this process enables fully automated identification of the regions where boundary conditions should be applied, based on

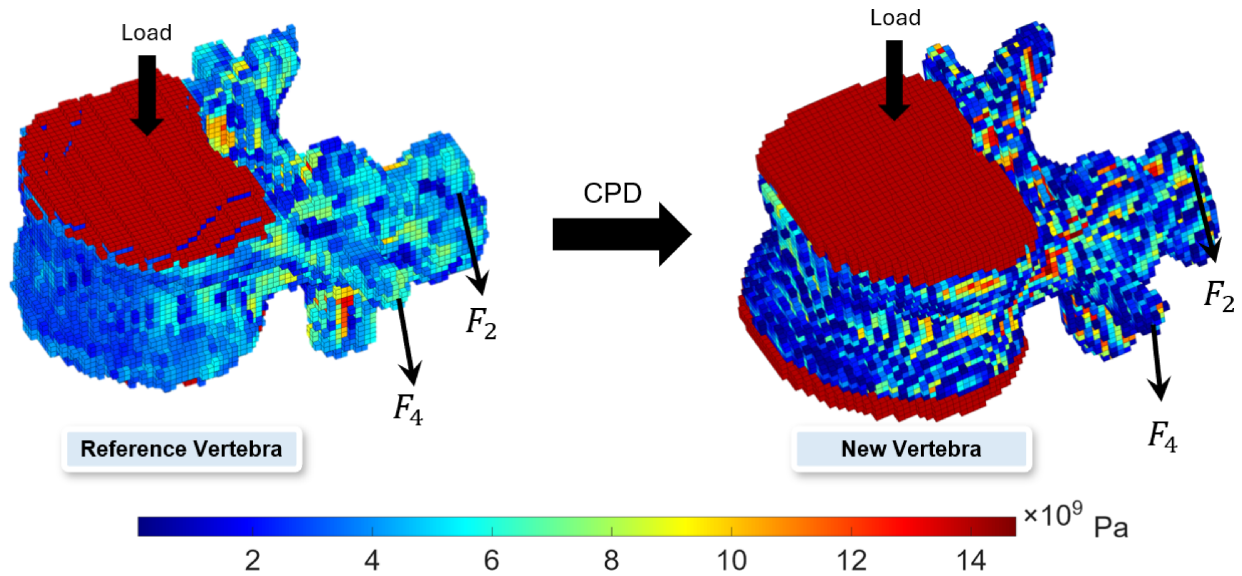


FIGURE 5 | Results of boundary conditions transference with CPD, from reference vertebra to new vertebra (Pa).

regions identified in the reference vertebrae. Figure 5 shows an example of the boundary conditions transferred by CPD from a reference vertebra to a new one, in addition to indicating in red the surface boundary conditions on the upper and lower parts of the main body of the vertebrae.

However, it should be noted that, although CPD enables the transfer of boundary-condition regions between vertebrae, its use must be accompanied by a validation procedure, as described in Section 3.2. This validation is required to assess the accuracy of the transferred regions and to ensure the appropriate definition of the boundary conditions.

2.2.3 | Online Workflow: Finite Element Model and Tumor Parametrization

The generation of finite element models is a key step for simulations using cgFEM. This begins with the vertebra models, similar to that shown in Figure 3. These models consist of the segmented vertebrae's voxels, with identified regions representing the inter-vertebral discs and muscle insertion areas.

The meshing of these geometries follows the method described in Ref. [21] (Figure 13), using linear elements with side length $h = 2.12$ mm, each comprising $2 \times 2 \times 2$ voxels. This choice is consistent with the refinement range identified in Ref. [21] for image-based analyses with linear interpolation. In that work, refining the mesh below a few voxels per element does not lead to the expected improvement in the finite element solution, since the modelling error associated with the voxelised representation becomes increasingly relevant. As the mesh is further refined, the convergence curves depart from the theoretical behaviour of the corresponding continuous problem and the numerical response becomes more strongly influenced by the singularities inherent to the voxelised model.

For this reason, the selected discretization of $2 \times 2 \times 2$ voxels was adopted as a solution, as it is sufficiently fine to retain

the image-derived material heterogeneity, while avoiding an over-refined representation.

Additionally, the vertebral material is considered isotropic, both for cortical and trabecular bone, with heterogeneous properties determined per voxel from its Hounsfield Unit (HU) value in the medical image. The material property equations are derived from [36, 37]:

$$BMD = 0.7574 \cdot \gamma + 0.5305 \quad (1)$$

$$\rho_{ash} = 9.53 \cdot 10^{-4} \cdot BMD + 0.0457 \quad (2)$$

$$\rho_{app} = \frac{\rho_{ash}}{0.6} \quad (3)$$

$$E = 4730 \cdot \rho_{app}^{1.56} \quad (4)$$

Here, BMD is the bone mineral density in g/cm^3 , γ are the voxel Hounsfield values, E is the Young's modulus in MPa, and the Poisson's ratio is assumed to be $\nu = 0.3$.

With all of these it is already possible to apply the cgFEM to the vertebra model. However due to the work focusing in the prediction of the fracture by metastasis, an artificial tumor is inserted into the vertebra to assess how its presence affects structural behavior and to quantify fracture risk. As in [38–40], tumors are modeled as spheres located in the vertebral body, which is the most common site for spinal metastases [41].

The artificial bone metastasis is defined by altering the Hounsfield values of voxels within a spherical region. This tumor model is defined by the parameters: ρ (tumor center density), R (spherical tumor radius), and $X_0 = x, y, z$ (tumor center coordinates). Density variation is represented by HU changes, which alters the material properties, allowing simulation of lytic tumors ($HU = 50-220$) or blastic tumors ($HU = 500-900$) [42, 43]. However, in order to ensure a more realistic transition between the tumor and the bone, a Gaussian filter is applied to the Hounsfield unit values of the voxels surrounding the tumor.

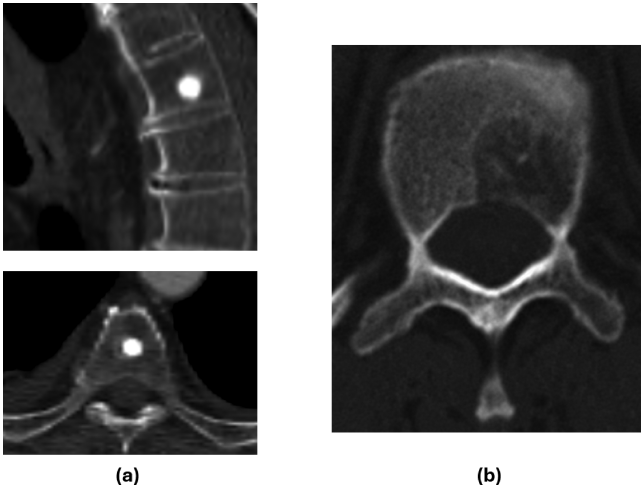


FIGURE 6 | Representation of tumors of different nature with varying transitions in the vertebral material. (a) C5 vertebra with a solid blastic tumor exhibiting a smooth transition within the vertebra, shown in axial and lateral views. (b) T11 vertebra with a lytic tumor exhibiting a thin transition within the vertebra, shown in axial view.

This transition not only enhances the overall realism of the model but also helps prevent potential instabilities caused by abrupt changes in density.

The artificial bone metastasis is defined by altering the Hounsfield values of voxels within a spherical region. This tumor model is defined by the parameters: ρ (tumor center density), R (spherical tumor radius), and $X_0 = x, y, z$ (tumor center coordinates). Density variation is represented by HU changes, which alters the material properties, allowing simulation of lytic tumors (HU = 50–220) or blastic tumors (HU = 500–900) [42, 43]. However, in order to ensure a more realistic transition between the tumor and the bone, a Gaussian filter is applied to the Hounsfield unit values of the voxels surrounding the tumor. Since the thickness of this transition region cannot be assumed to be constant, it should be considered as a patient-specific parameter, and potentially even tumor-specific. This transition enhances the overall realism of the model, helping to better reproduce the appearance observed in medical imaging and to account for the diffuse patterns often present in certain metastatic lesions (see Figure 6). In this way, the model can represent both well-defined (solid) tumors and cases exhibiting smoother transitions between the tumor and the surrounding bone tissue.

To apply the Gaussian filter, once the voxels corresponding to the defined tumor have been selected, a new parameter, R_{Gauss} , is introduced, representing the radius of the Gaussian filter's shell. The influence of this parameter on the results is evaluated through a sensitivity analysis, as described in Section 3.3. With both R and R_{Gauss} defined, any voxel located between these two radii will have its density value ρ_i modified. In this transition zone, ρ_i is computed through a weighted interpolation between its original value $\rho_{i,ini}$ and the result of a Gaussian distribution $\rho_{i,Gauss}$, which varies between the tumor density ρ_0 and the value $\rho_{i,R}$, associated with the voxel closest to the outer layer of R_{Gauss} . The updated ρ_i is then calculated based on the voxel position X_i

relative to the tumor center, using the following formulation:

$$\rho_i = N_1 \rho_{i,Gauss} + N_2 \rho_{i,ini} \quad (5)$$

$$N_1 = \frac{R_{Gauss} - |X_i|}{R_{Gauss} - R} \quad (6)$$

$$N_2 = \frac{|X_i| - R}{R_{Gauss} - R} \quad (7)$$

Additionally, $\rho_{i,Gauss}$ is computed as a Gaussian distribution, whose standard deviation for blastic and lytic cases is calculated as follows:

$$\sigma_{bl} = \frac{R_{Gauss} - R}{\sqrt{-2 \ln\left(\frac{\rho_{i,R}}{\rho_0}\right)}} \quad (8)$$

$$\sigma_{lyt} = \frac{R_{Gauss} - R}{\sqrt{-2 \ln\left(\frac{\rho_{i,R}}{2\rho_{i,R} - \rho_0}\right)}} \quad (9)$$

Figure 7 illustrates the tumor parameters on a vertebra and the R_{Gauss} radius of the tumor.

The next step is the application of the Cartesian Grid Finite Element Method (cgFEM) [27], which allows structural analysis of the tumor-affected vertebra directly from its voxel data, without requiring a CAD model. The cgFEM analysis yields displacement and stress fields within the vertebra, with an average analysis time of 40 s.

2.2.4 | Online Workflow: Fracture Criteria

Once the displacement and stress fields are obtained for a tumor-affected vertebra, defined by the parameters $\{\rho, R, x, y, z\}$, the next step in predicting vertebral fracture is defining a failure criterion to identify voxels where fracture occurs.

Among the most commonly used failure criteria in bone fracture analysis are: the Mohr-Coulomb criterion, for isotropic materials with differing tensile and compressive behaviors; the Hoffman criterion, for brittle materials; and the Von Mises-Hencky criterion, which assumes equal tensile and compressive limits [44].

Any of these, or any other structurally-based criterion developed in the future, can be used to determine vertebral fracture risk. For demonstration purposes, this work adopts the Von Mises-Hencky criterion. It's important to note that this criterion may not be fully appropriate, as it is typically used for yielding failure and assumes equal absolute tensile and compressive strengths, which is not realistic. Nevertheless, due to its simplicity and reliability, Von Mises is one of the most commonly used fracture risk estimators in the literature [44–46].

This failure criterion is applied to each voxel in the analyzed vertebrae, allowing computation of a safety factor against bone failure. The Von Mises-Hencky safety factor is calculated as follows:

$$X = \frac{\sqrt{(\sigma_1 - \sigma_2)^2 + (\sigma_2 - \sigma_3)^2 + (\sigma_3 - \sigma_1)^2}}{\sigma_c} \geq 1 \quad (10)$$

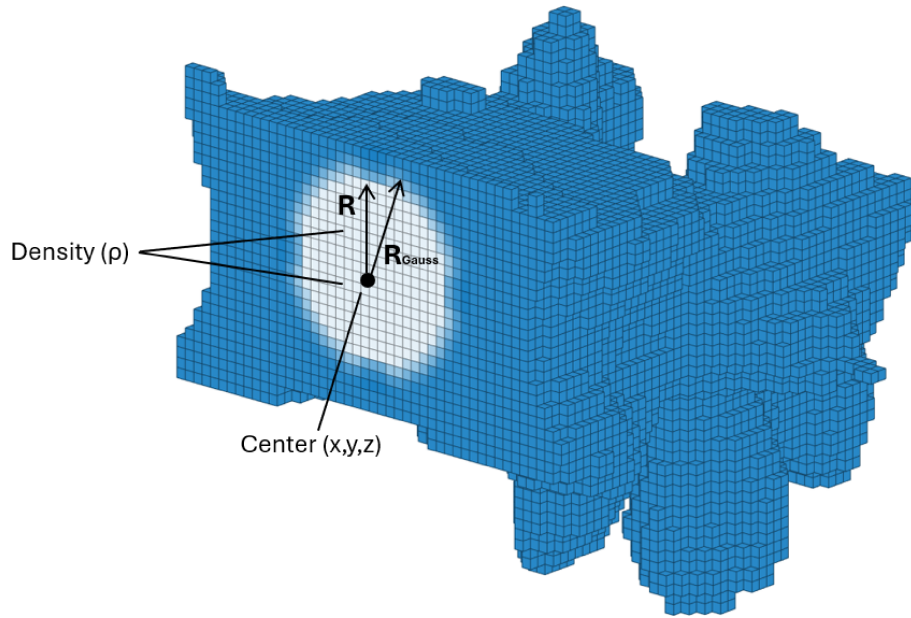


FIGURE 7 | Example of a parameterized tumour representation, identifying the variables defined for the generation of the metastasis.

Here, σ_1 , σ_2 , and σ_3 are the principal stresses at the voxel center, and σ_c is the critical compressive stress for that voxel's density values obtained from the literature [44] and this formula:

$$\sigma_c = 117 \cdot \rho_{ash}^{1.97} \quad (11)$$

Here ρ_{ash} is the ash density of the voxel center, obtained from the Equation (2).

3 | Validation

This section presents a systematic analysis and validation of several methodologies employed within the proposed pipeline. The primary objective is to assess their robustness and suitability for the intended application.

3.1 | Semantic Segmentation Validation

Once the semantic segmentation workflow has been defined through the training of different neural network models, it is necessary to validate the overall process by applying it to a set of spinal columns not included in the training dataset and by analyzing the results through comparison between the manually generated masks and the automatically segmented ones. For this purpose, 10 CT scans, previously segmented manually, were processed using the segmentation software in order to obtain automatic vertebral segmentations and evaluate the performance of the trained models.

To evaluate segmentation accuracy, the predicted masks are compared to their ground truth (i.e., the original database mask), and segmentation quality metrics are calculated. Four metrics are considered:

- DICE coefficient: measures similarity between two samples

TABLE 2 | Validation results for semantic vertebral segmentation on a set of spinal columns not included in the training dataset.

Dice coef.	0.9536
Precision	0.9525
True pos.	0.9549
True neg.	0.9498

- Precision: proportion of correct model predictions relative to total predictions
- True Positive: proportion of actual positive cases that the model correctly predicted as positive.
- True Negative: proportion of actual negative cases that the model correctly predicted as negative.

Table 2 presents the median values of the proposed metrics for the validation dataset.

The results reported in Table 2 indicate that the proposed semantic segmentation approach achieves a high level of agreement with the manual annotations on spinal columns that were not included in the training dataset. In particular, the mean Dice coefficient of 0.9536 suggests a strong overlap between the predicted masks and the ground-truth masks, while the precision of 0.9525 indicates that most of the voxels identified by the model as belonging to the vertebrae were correctly classified. Similarly, the true positive and true negative values, both around 0.95, show that the model is able to accurately identify both vertebral and non-vertebral regions. Taken together, these results support the ability of the trained networks to generalize to unseen cases while maintaining a high segmentation quality.

Additionally, to further support the evaluation of the segmentation results, a qualitative visual comparison was conducted

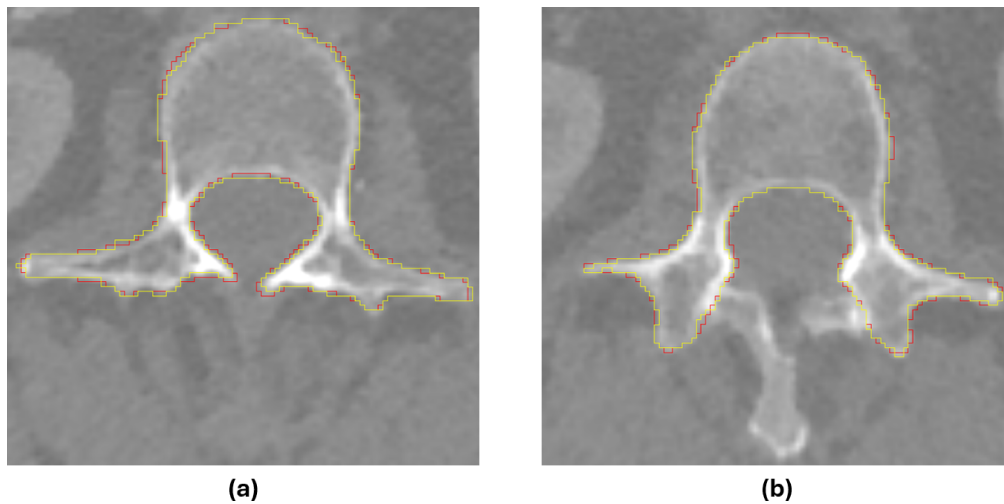


FIGURE 8 | Overlay of the vertebral masks on the medical image for different slices. The manually generated reference mask is shown in yellow, whereas the mask predicted by the neural network is shown in red. Panels (a) and (b) show two different slices of the medical image.

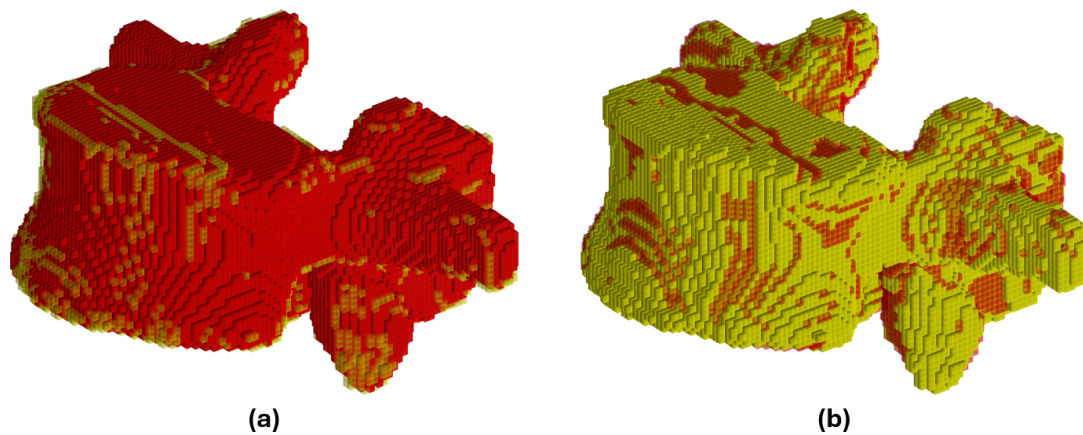


FIGURE 9 | Three-dimensional comparison of the masks for the selected vertebra. The reference mask is shown in yellow, whereas the mask predicted by the neural network is shown in red. (a) Superposition of the predicted mask onto the reference mask. (b) Superposition of the reference mask onto the predicted mask.

between one automatically generated L1 vertebral mask and the corresponding reference mask. This assessment was performed using two complementary approaches: the overlay of both masks on selected medical image slices and the comparison of their corresponding three-dimensional representations. The results of these visual comparisons are shown in Figures 8 and 9.

As shown in Figure 8, the superposition of the mask contours on the medical image makes it possible to identify the origin of the discrepancies observed in the quantitative metrics. In these examples, both the reference and predicted masks aim to closely fit the vertebral contour and generally follow similar spatial patterns. However, it can also be observed that the predicted mask (red) includes some boundary voxels as part of the bone, even though these voxels do not strictly belong to the original vertebral structure. As a result, a limited number of voxels not belonging to the bone may be incorporated into the generated model.

Nevertheless, these voxels are located in boundary regions and exhibit mechanical properties different from those of cortical

bone. For this reason, their effect on the subsequent biomechanical analyses is limited.

Furthermore, it should be noted that in Figure 8b, the generated mask does not include the transverse process observed in the lower part of the image, since this structure belongs to a different vertebra. This demonstrates the ability of the network to differentiate between adjacent vertebrae.

In addition, Figure 9 shows the three-dimensional superposition of the masks, where each voxel is represented as a cube in space. In this representation, the manually generated original mask is shown in yellow, whereas the predicted mask is shown in red. In superposition (a), the predicted mask is placed over the original mask, making it possible to identify missing voxels as yellow cubes. Although such voxels appear in specific local regions, their number is limited and they are therefore unlikely to substantially affect the structural analysis. In superposition (b), the original mask is placed over the predicted mask, allowing the identification of additional selected voxels as red cubes. As discussed in

Figure 8, these voxels may lead to the inclusion of tissues outside the vertebral structure in the model; however, their impact on the analysis is limited.

Taken together, these qualitative comparisons support the validity of the automatic segmentation results and indicate that the predicted masks provide a sufficiently accurate representation of the vertebral geometry for the purposes of the present study.

3.2 | CPD Validation

As discussed in Section 2.2.2, the use of CPD enables the automatic transfer of boundary conditions from a reference vertebra to a new patient-specific vertebra, without requiring manual intervention. However, although the transferred boundary conditions appear visually consistent, as shown in Figure 5, an accuracy assessment was performed by comparing the CPD-based placement with a manually defined reference placement.

The comparison was mainly focused on the point forces, since these boundary conditions are more sensitive to potential inaccuracies in the CPD registration process. In contrast, surface boundary conditions are expected to be less affected by local registration errors, as they are defined by a set of points that are used to determine a surface region. Therefore, an error in the position of an individual point is unlikely to substantially affect the overall definition of the surface boundary condition. The comparison was carried out using two complementary approaches: a visual assessment of the locations of the predicted and manually placed forces, as shown in Figure 10, and a quantitative analysis based on the distances between the CPD-predicted points and the corresponding manually defined points.

As shown in Figure 10, the position of the boundary conditions obtained using CPD is highly consistent with the manually defined placement, supporting the visual validation of the CPD-based transfer procedure. To further evaluate these results, the distances between the CPD-transferred force application points and the manually defined reference points were computed.

This analysis showed that the CPD-based force application points were located at a mean distance of 2.9 mm from the corresponding manually defined points, with a standard deviation of 0.31 mm. These results indicate that the transferred points remain close to the manual reference placement, supporting the accuracy of the proposed approach for the automated definition of point-force boundary conditions.

3.3 | Gaussian Filter Validation

Section 2.2.3 described the procedure for generating an artificial tumor within the vertebral bone, including the use of a Gaussian filter whose purpose is to improve the appearance observed in medical imaging and to account for the diffuse patterns often present in certain metastatic lesions. In this section, the sensitivity of this parameter is evaluated by considering different Gaussian radius sizes, with the aim of determining the extent to which its value influences the analyses.

The study was conducted on a vertebra in which a lytic tumor was generated, affecting both cortical and trabecular tissues.

For this analysis, the Gaussian radius was defined as a function of the voxel size used in the model and the radius of the simulated tumor (see Equation (12)).

$$R_{Gauss} = R + V_{Size} \cdot N_{voxel} \quad (12)$$

In this expression, R denotes the radius of the simulated tumor, V_{Size} is the voxel size used in the finite element analysis, and N_{voxel} is the number of voxels defining the thickness of the Gaussian transition layer. In the present study, values of N_{voxel} ranging from 0 to 3 were investigated, both visually and numerically, through comparison of Von Mises stress results inside the tumor and in the outer layer closest to the tumor boundary.

The corresponding Von Mises stress results are shown in Figure 11.

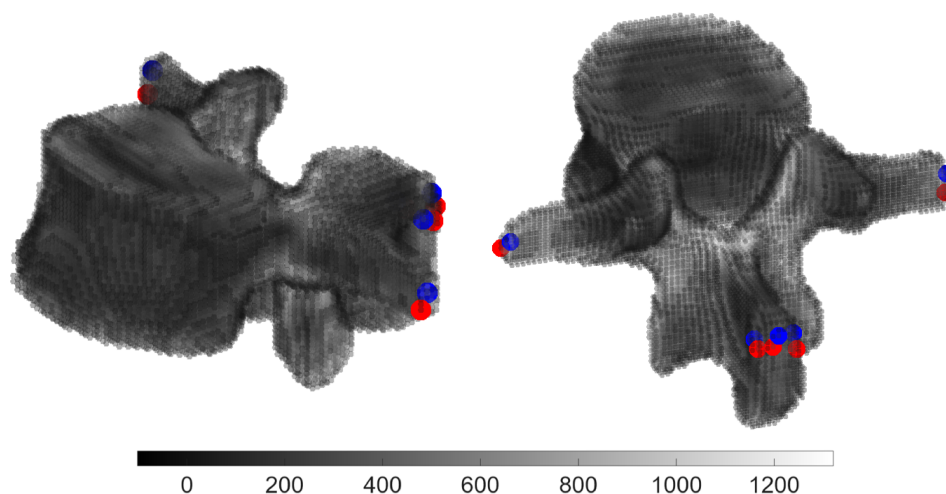


FIGURE 10 | Three-dimensional representation of a vertebra with the manually defined boundary conditions shown in blue and the CPD-transferred boundary conditions shown in red.

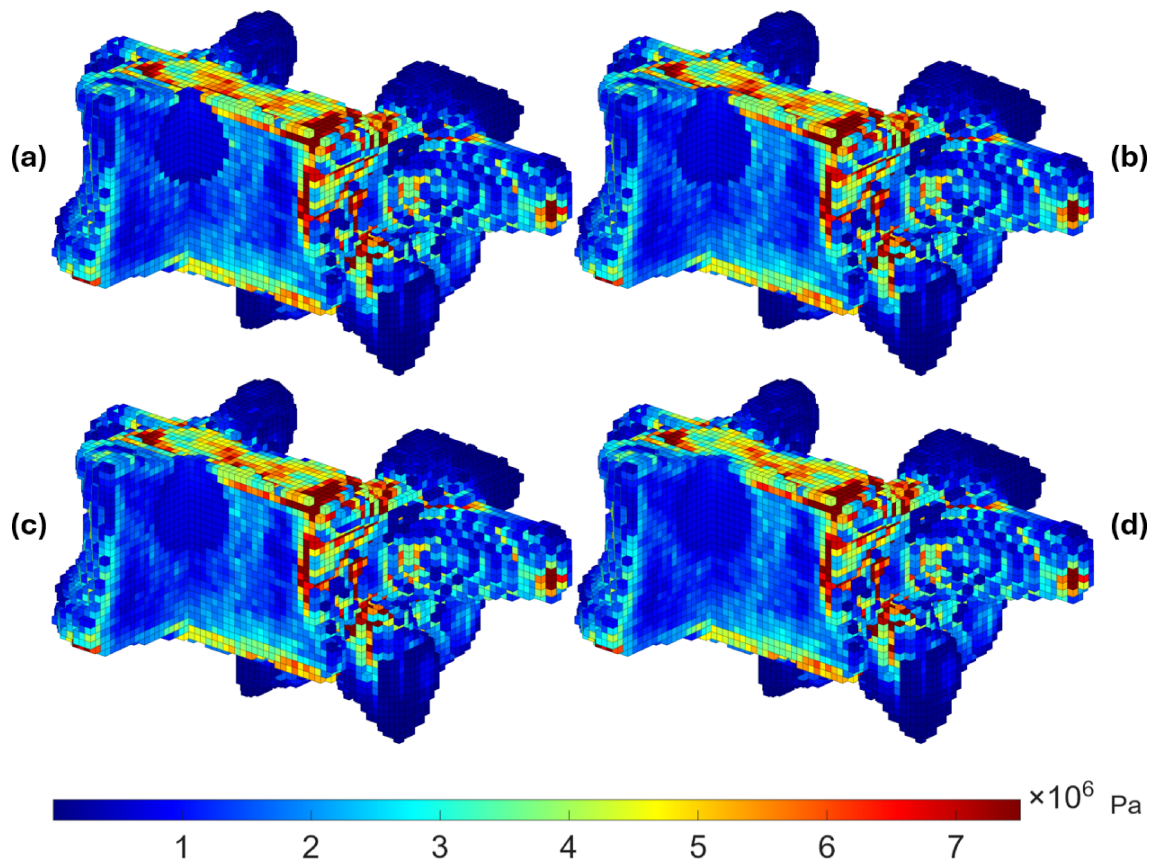


FIGURE 11 | Von Mises stress distributions obtained for a vertebra with different Gaussian filter sizes applied. (a) $N_{\text{voxel}} = 0$. (b) $N_{\text{voxel}} = 1$. (c) $N_{\text{voxel}} = 2$. (d) $N_{\text{voxel}} = 3$.

As can be observed in Figure 11, for the smaller transition sizes ($N_{\text{voxel}} = 0$ and 1), stress concentrations appear in the vicinity of the tumor, particularly in the cortical tissue, which suggests non-physical numerical artifacts associated with abrupt material changes. In contrast, for transition sizes of $N_{\text{voxel}} = 2$ and 3, the stress field appears smoother near the tumor boundary, reducing the presence of stress concentrations and providing a more physically consistent response.

Additionally, a quantitative comparison of the Von Mises stress values inside the tumor and in the outer layer of the Gaussian radius was performed in order to assess the minimum filter radius required to avoid the generation of numerical artifacts. For each Gaussian radius, point-wise stress differences were computed between the outer tumor boundary and the nearest corresponding points in the immediately surrounding external layer. The mean percentage difference obtained for each transition size is summarized in Table 3.

The results show that the Gaussian transition thickness has a clear influence on the stress distribution at the tumor-bone interface. In the absence of a transition region ($N_{\text{voxel}} = 0$), the mean Von Mises stress difference between the tumor boundary and the surrounding external layer was 66.82%, indicating a marked stress discontinuity caused by the abrupt change in material properties. When a Gaussian transition was introduced, this difference decreased substantially, reaching 24.33% for one voxel, 10.01% for two voxels, and 7.33% for three voxels.

TABLE 3 | Analysis of Gaussian transition thickness based on Von Mises stress differences between the tumor boundary and the surrounding external layer.

N_{voxel}	Mean difference (%)
0	66.82
1	24.33
2	10.01
3	7.33

These findings indicate that the model is sensitive to the Gaussian radius, particularly when comparing the absence of smoothing with the inclusion of a transition layer. Increasing the transition thickness progressively reduces the stress discontinuity, leading to a smoother mechanical response across the tumor-bone interface. Therefore, this parameter may also contribute to the personalization of patient-specific models, since not all tumors develop in the same manner or present the same degree of transition with the surrounding bone tissue. Adjusting the Gaussian transition thickness allows the model to better represent different tumor-bone interfaces, which may vary depending on the characteristics and progression of each lesion.

Based on both qualitative and quantitative criteria, a Gaussian transition thickness of 3 voxels was selected for the sample analyzed in this paper.

4 | Results

This section presents an example application of the proposed methodology on a CT scan from a healthy patient, focusing on one of their lumbar vertebrae to assess its structural stability in the presence of a simulated artificial tumor and its comparison to the biomechanical response of the original healthy vertebra.

4.1 | Column Segmentation

As discussed in Section 2, the first step of the developed methodology for vertebral structural analysis is the semantic segmentation of the CT scan to which it belongs. The spine used for analysis comes from the same dataset used for training the Deep Neural Network [28, 29], but it belongs to the validation group and was not used for training any of the networks. This enables comparison of the final predicted masks with the ground truth to evaluate the Deep Learning model's accuracy.

Figure 12 shows the results obtained from each trained model and the final segmentation masks for each vertebra.

Once the spine has been semantically segmented, the obtained masks are used to extract vertebra models from the CT scan. The selected vertebra for FE analysis is vertebra L1, and in order to evaluate the segmentation accuracy, the predicted mask of vertebra L1 is compared to its ground truth using the metrics considered in Section 3.1. The comparison results are shown in Table 4.

As shown in Table 4, the metrics reach high values, indicating strong model performance in segmenting vertebra L1. The high

TABLE 4 | Metrics results from L1 vertebra.

Dice coef.	0.958
Precision	0.942
True pos.	0.975
True neg.	0.982

Dice coefficient confirms good overlap between predicted and reference masks, while high precision reflects few false positives. Moreover, the elevated true positive and negative values suggest high sensitivity and specificity. These results validate the model's reliability for automatic segmentation of vertebra L1, illustrated in Figure 13.

4.2 | CPD and Boundary Conditions Creation

Once the geometric model of vertebra L1 has been obtained and normalized (as described in Section 2.2.2), the next step involves applying CPD. The reference vertebra used is the L1 defined in the offline phase, which has predefined boundary conditions (Section 2.1.2).

Two point clouds are created from the reference and L1 vertebrae and used as input for the CPD algorithm. As described in Section 2.2.2, CPD is applied in two stages: a rigid transformation to reorient and align the reference vertebra, and a non-rigid transformation to deform the geometry and adapt it to the target vertebra.

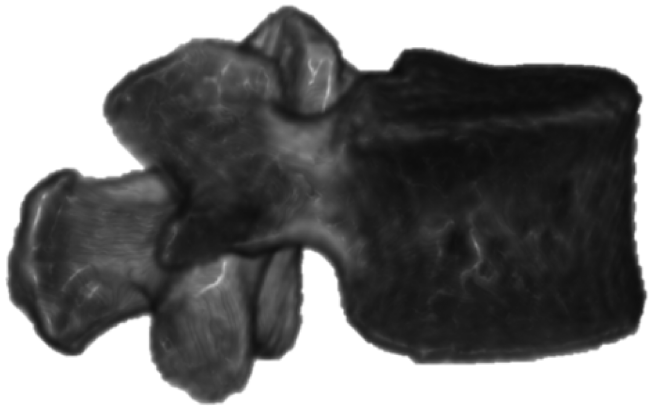


FIGURE 13 | Results obtained for an L1 lumbar vertebra using the semantic segmentation pipeline.

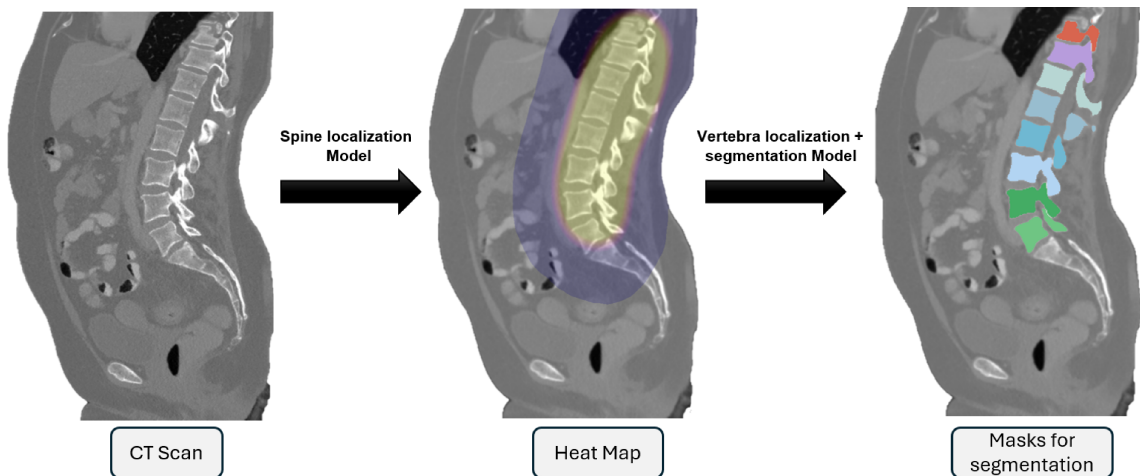


FIGURE 12 | Application of the semantic segmentation framework and corresponding results. From the original CT scan, the spine localization model produces a heatmap indicating the location of the spinal column, and the vertebra localization and segmentation models are subsequently used to identify and extract the vertebral masks.

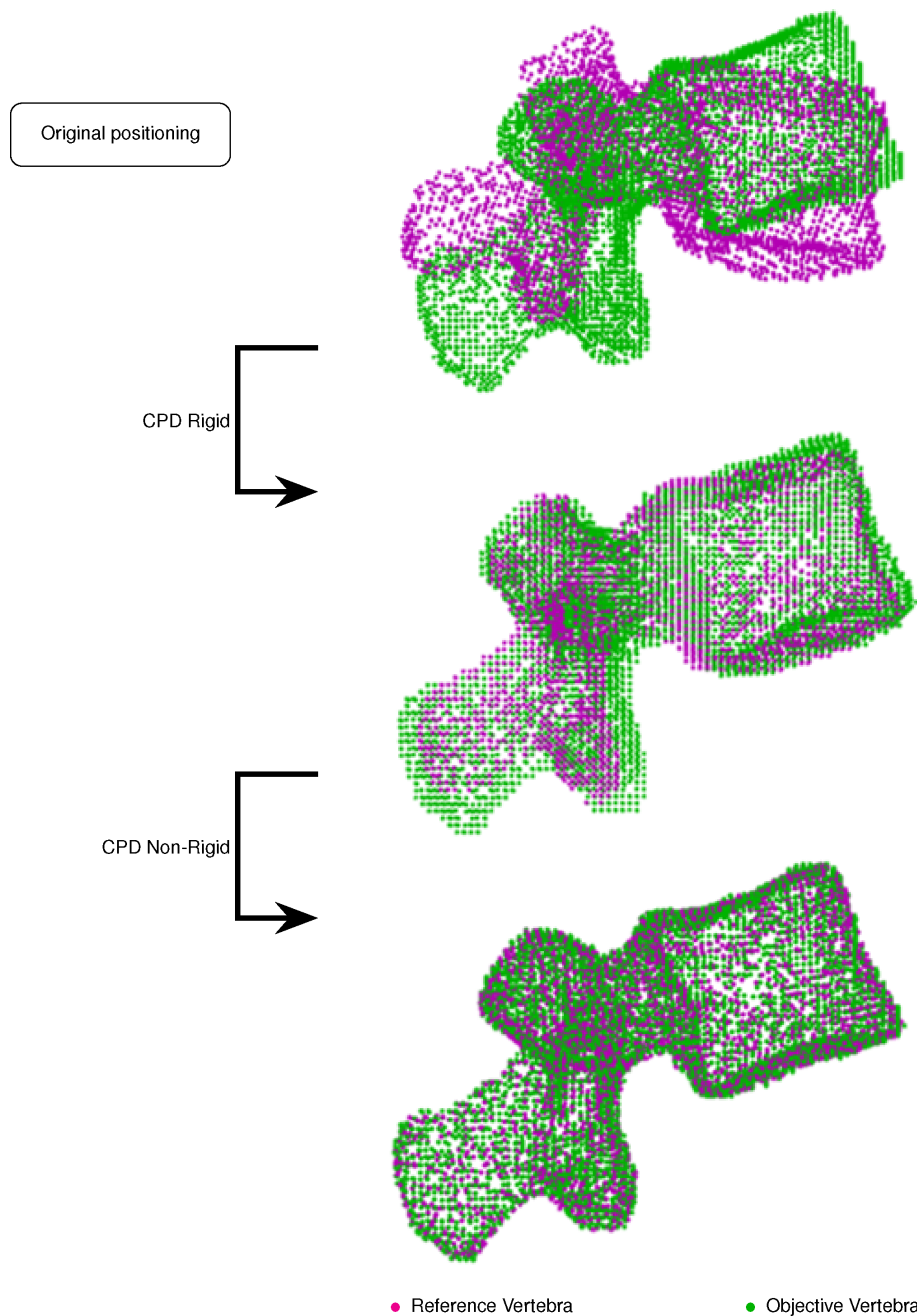


FIGURE 14 | Coherent Point Drift (CPD) transformation applied to the patient-specific vertebra. The first point cloud comparison corresponds to the initial positioning of the vertebrae. The second point cloud shows the result after applying rigid CPD to the initial configuration. The third point cloud presents the final result obtained after applying non-rigid CPD to the rigidly aligned model.

Figure 14 shows the results of the CPD rigid and non-rigid transformations.

Once both point distributions are aligned, boundary conditions are automatically transferred to the target vertebra. The final BC applied to vertebra L1 is shown in Figure 15.

4.3 | Tumor Generation

With the vertebra model and boundary conditions established, the next step is defining the characteristics of the simulated

tumor to perform the finite element analysis. Specifically, three different artificial tumors are simulated with the same density and location, varying only the radius to mimic tumor growth inside the vertebra. The parameters used are shown in Table 5.

The original healthy vertebra, together with the simulated tumor Hounsfield values and their corresponding regions of influence within the vertebra, are illustrated in Figure 16.

As can be observed in Figure 16, the selected Radius dimensions for the vertebra analyses simulate the growth of a tumor until it

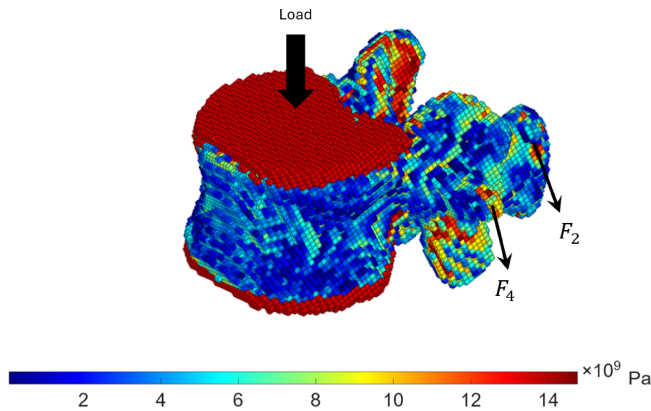


FIGURE 15 | Localization of the boundary conditions on an L1 lumbar vertebra after application of the Coherent Point Drift algorithm. (Young Modulus, Pa).

TABLE 5 | Tumor simulation parameters.

Lytic tumor [HU]	50
x, y, z [mm]	85,65,55
R [mm]	3.2–9.5–15.9

eventually affects the cortical tissue of the body, which is responsible for maintaining the structural stability of the vertebra. This would represent a critical situation for the vertebral structure.

Having generated the vertebra model and established the metastatic cases to be analyzed, the cgFEM is used for mesh generation and subsequent finite element (FE) analysis, allowing for the evaluation of the structural stability of the vertebra in each case and the application of the selected failure criterion.

4.4 | Stress and Strain Field Analysis

Once the vertebral model had been obtained and the metastatic cases to be analyzed had been defined, all the required information was introduced into the cgFEM framework. The finite element models were then solved to obtain the displacement field, enabling the analysis of mechanical response metrics such as Von Mises stress and strain for both the metastatic and healthy cases.

Additionally, the tumor growth model was evaluated on a finite element model of the same vertebra generated from a manually created mask, with boundary conditions also defined manually. This additional analysis was performed in order to assess the performance of the automated process by comparison with a more user-defined setup.

The determination of the stress and strain fields enables the identification of regions that are most structurally affected by variations in bone density, which may indicate critical points susceptible to fracture.

Figures 17 and 18 illustrate the effects of the different simulated metastases on the Von Mises stress and strain distributions. For

comparison purposes, in each figure the results are presented in separate columns, distinguishing between the automatically generated finite element model and the manually generated model. Additionally, the figures corresponding to the first and third deformation modes of the automated process have been included as Supporting Information (S1 and S2).

The simulation of different tumors within the vertebra results not only in changes in bone density, but also in variations in the Von Mises stress distribution and an increase in the strain field in the affected region, which could potentially contribute to vertebral fracture.

Additionally, as observed from the comparison between the automatically generated model and the manually generated model, both approaches provide highly similar results. The differences are mainly limited to a few external voxels that were not segmented by the neural network, together with very slight numerical variations in the computed mechanical fields. These findings indicate that the automated process is capable of accurately reproducing the behavior obtained with the manually generated model, while considerably reducing the need for human intervention and the associated model preparation time.

4.5 | Fracture Criteria Analysis

With the stress field computed, the final step is applying the Von Mises-Hencky failure criterion defined in Section 2.2.4. The failure criterion allows for the identification of potential regions where structural failure of the vertebra could occur due to the simulated metastases, as a result of a significant reduction in the safety factor.

Figure 19 shows the results of the Von Mises-Hencky safety factor for each of the proposed cases. As in the previous analysis, the results obtained from the automatically generated model are compared with those from the manually generated model.

In the results obtained from the application of the Von Mises-Hencky failure criterion, isolated surface voxels with safety factor values lower than 1 can be observed. These voxels are mainly located near the vertebral boundary and do not form part of a continuous failure nucleus. Their presence is associated with the direct generation of the finite element model from CT images. Due to the inherent spatial discretization of CT data, some boundary elements may partially include bone and partially include surrounding soft tissue, leading to a transition layer of low-density voxels along the vertebral contour.

This effect is acknowledged as a limitation of the current approach. A more aggressive segmentation strategy, excluding low-density voxels from the analysis, could reduce the presence of these boundary-related artefacts. However, this would also modify the CT-derived vertebral geometry and could remove peripheral bone regions. Therefore, a trade-off exists between preserving the original CT-based geometry and reducing artefacts associated with the bone boundary.

In the present study, the actual material property is considered and the inclusion of these voxels in the analysis does not affect

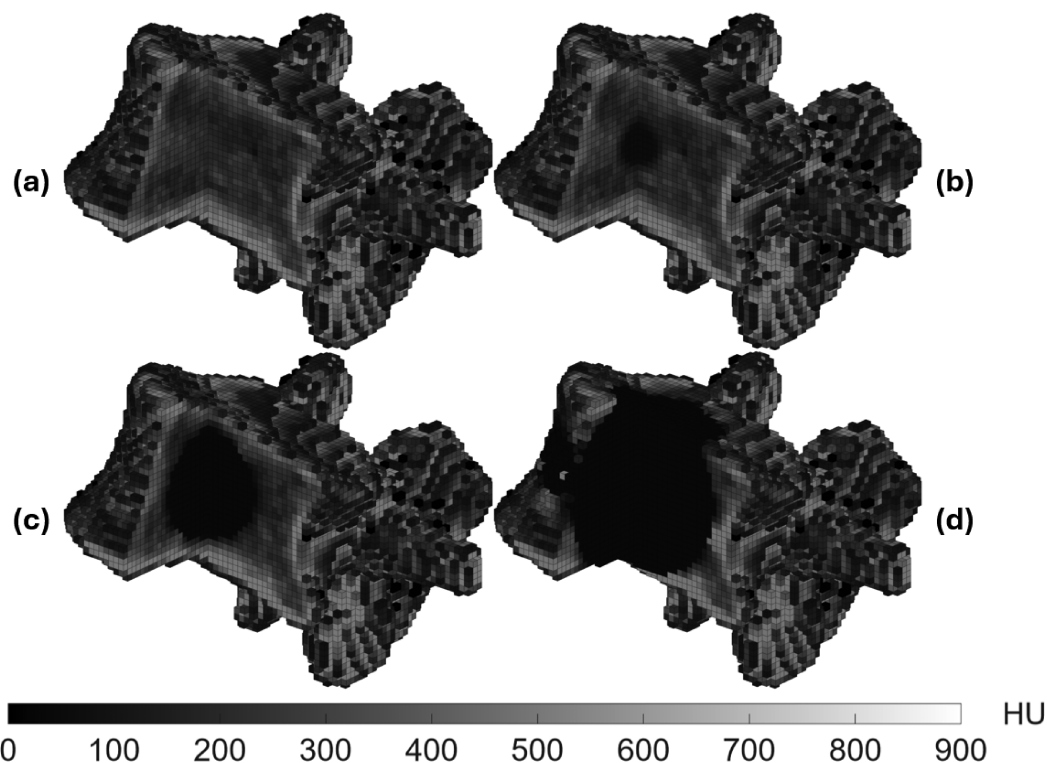


FIGURE 16 | Distribution of Hounsfield units (HU) in an L1 vertebra under different lytic tumour scenarios. (a) Healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, (d) $R = 15.9$ mm.

the global results since the stiffness addition is weighted by the material properties limiting their influence on the overall mechanical response. Nevertheless, isolated surface voxels with safety factor values below 1 should be interpreted with caution and should not be considered, by themselves, as evidence of vertebral failure. To prevent these isolated boundary artefacts from influencing the assessment of fracture, a cluster-based criterion was adopted. Thus, vertebral fracture was only considered to occur when a continuous cluster of voxels indicating failure was present. In this study, clusters of 15 contiguous voxels were used as the reference threshold.

As shown in Figure 19, the simulation of tumors with small radius affecting only the trabecular region does not produce an apparent structural failure in the vertebra, indicating that trabecular bone has limited influence on the overall structural stability of the vertebra. However, as the radius of the metastasis increases and begins to affect the cortical tissue, critical failure regions start to appear, as indicated by safety factor values falling below 1. This occurs because cortical bone is primarily responsible for maintaining the structural stability of the vertebra. Consequently, a reduction in density within this layer may lead to bone fracture, confirming that the numerical results accurately simulate the impact of metastasis on vertebral stability.

Furthermore, similarly to the stress and strain field comparisons, the safety factor distributions obtained from the automatically generated model show a high degree of agreement with those obtained from the manually generated model. The observed differences are minimal and mainly associated with small segmentation inaccuracies in external regions, demonstrating that the

automated workflow is capable of providing reliable predictions of vertebral failure without the need for extensive manual intervention.

Of course, this is a simple failure model based on the Von Mises-Hencky criterion. Since the full elastic solution (displacement, strains, and stresses) is available, any other failure model of interest to the user can also be implemented.

5 | Discussion

This study presents a fully automated, patient-specific methodology for predicting the risk of structural failure in vertebrae affected by metastasis, with the potential to support clinical decision-making and treatment planning.

The generation of vertebral models for Finite Element Analysis (FEA) is achieved through a deep neural network structured into three functional blocks, designed for the identification and semantic segmentation of individual vertebrae from CT images. This segmentation process achieves high accuracy across multiple metrics (Table 4), enabling its use without the need for manual intervention. However, after segmentation, differences may exist in reference systems and positioning between different CT studies, caused by both the scanning equipment and the patient's posture. These differences hinder the execution of finite element analysis and compromise full workflow automation.

To overcome this issue, a vertebral normalization step is integrated into the pipeline, ensuring consistent orientation and

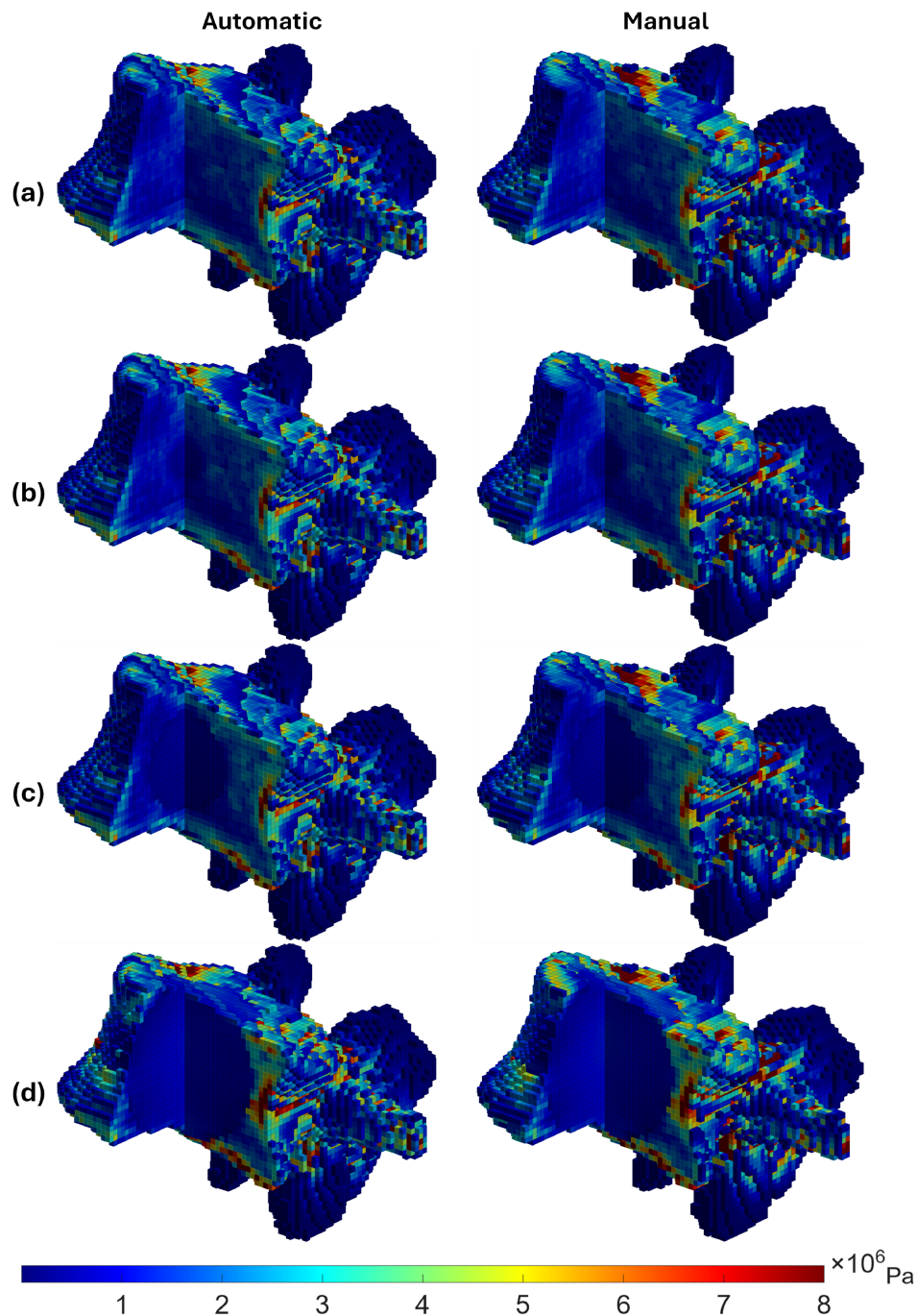


FIGURE 17 | Von Mises stress distribution (Pa) in an L1 vertebra for different lytic tumour scenarios, comparing the automatically generated model with the manually generated model. (a) Healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, (d) $R = 15.9$ mm.

scaling of the vertebral models. Furthermore, the inclusion of the Coherent Point Drift (CPD) algorithm facilitates the automatic definition of boundary conditions across varying vertebral geometries, thereby preparing the models for FEA without requiring user input.

The FEA are performed using the Cartesian Grid Finite Element Method (cgFEM), which enables efficient prediction of vertebral mechanical behavior in only 40 s per analysis. In particular, the estimation of the safety factor allows for the evaluation of structural integrity under pathological conditions. The simulation of a spherical tumor, with variable size, location, and

density, enables comprehensive assessment of how different metastatic configurations influence vertebral stability. This level of analysis provides valuable insights that can support clinicians in selecting the most appropriate treatment for individual patients.

As a result, the proposed methodology enables end-to-end automation of the structural assessment process, from CT imaging to fracture risk evaluation, significantly enhancing the clinical information available for therapeutic decision-making and serving as a powerful tool in the management of patients with spinal metastases.

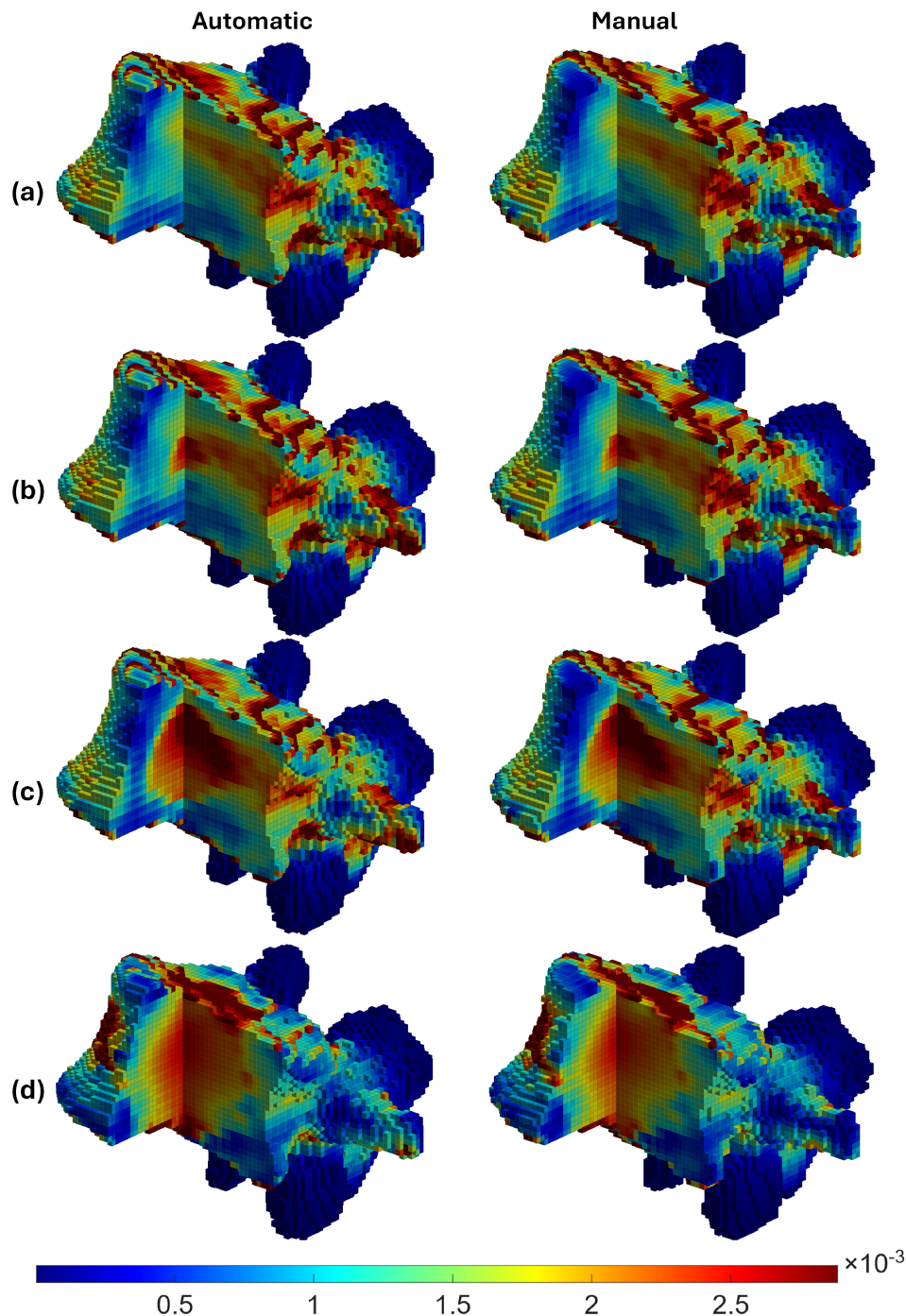


FIGURE 18 | Von Mises strain distribution in an L1 vertebra for different lytic tumour scenarios, comparing the automatically generated model with the manually generated model. (a) Healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, (d) $R = 15.9$ mm.

Nevertheless, although a computation time of 40 s per cgFEM analysis is relatively low and allows a large number of parametric studies to be performed within a few hours, it may still limit direct integration into routine clinical practice, where near real-time results are desirable. To address this limitation, the Sparse Subspace Learning (SSL) technique [47], a machine-learning-based approach proposed in Ref. [27], can be incorporated. SSL is a non-intrusive reduced-order modeling technique that enables interpolation of the results obtained from the parameterized model.

SSL relies on a hierarchical sampling strategy based on the Smolyak rule, which helps mitigate the difficulties commonly associated with sampling in high-dimensional parametric spaces. Consequently, it enables the construction of a surrogate model capable of approximating the structural response throughout the defined parameter space, with evaluation times of approximately 0.4 s. Such rapid response times support the potential clinical implementation of the proposed methodology, which could be used as a fast predictive tool to assess the risk of vertebral collapse under different tumour growth scenarios and provide valuable

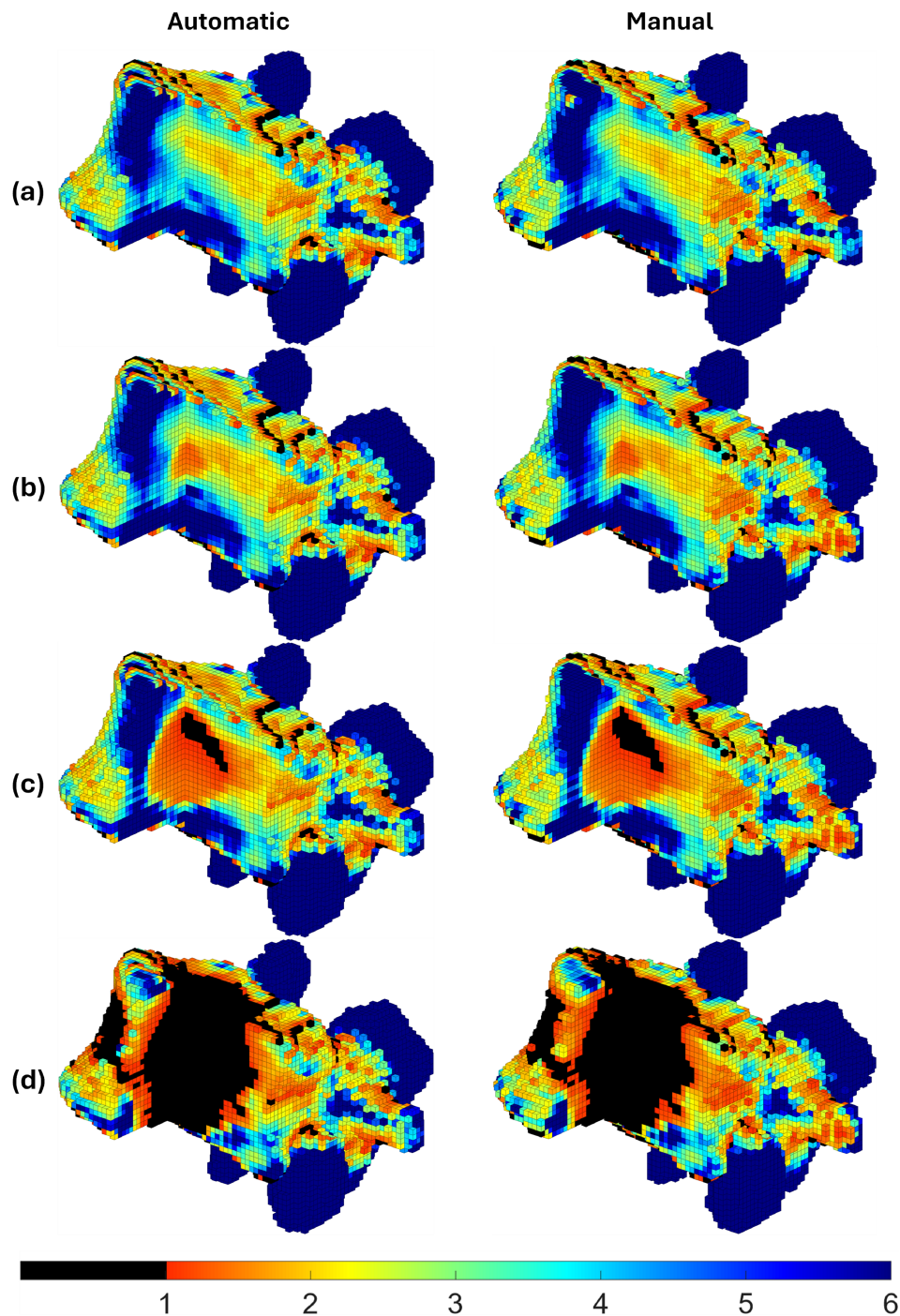


FIGURE 19 | Von Mises-Hencky safety factor in an L1 vertebra for different lytic tumour scenarios, comparing the automatically generated model with the manually generated model. (a) Healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, (d) $R = 15.9$ mm.

information for selecting the most appropriate patient-specific treatment.

Finally, although the proposed methodology provides valuable support for the study of vertebral structural behavior and contributes meaningfully to clinical decision-making and treatment planning, it presents several limitations. One of the main constraints lies in the use of fixed magnitudes for boundary conditions during the analysis, which limits the accuracy of the patient-specific models, as actual physiological loads can vary

significantly between individuals. Furthermore, the use of the 15 voxel threshold to identify potential fractures may lack precision and could lead to false positives in certain cases.

In light of these limitations, future research in this area could focus on two primary directions. First, the personalization of boundary conditions using patient-specific clinical data, with the aim of enhancing the physiological realism and predictive power of the structural analyses. Second, the development of a machine learning model trained on clinical history and

simulation outputs, capable of estimating vertebral collapse risk. Such a model could ultimately be integrated into a Clinical Decision Support System (CDSS), offering a more robust and data-driven tool for guiding treatment decisions in patients with spinal metastases.

6 | Conclusions

This work introduces a fully automated, patient-specific pipeline to predict the risk of structural failure in vertebrae affected by metastasis, with direct applicability to clinical decision-making and treatment planning. A deep-learning segmentation module achieves high accuracy and removes the need for manual intervention; subsequent vertebral normalization and CPD-based assignment of boundary conditions standardize models across CT studies. Leveraging cgFEM, the framework estimates safety factors and quantifies how variations in simulated tumors (size, location, and density) influence vertebral stability, yielding clinically interpretable metrics. Together, these components enable an end-to-end workflow, from CT imaging to fracture-risk evaluation, that can enhance the management of patients with spinal metastases.

Current limitations include the use of fixed-magnitude boundary conditions, which may limit physiological realism, and a 15-voxel threshold for potential fractures that could generate false positives. Future work will focus on personalizing boundary conditions with patient-specific clinical data and on developing a predictive model that integrates clinical history with simulation outputs, ultimately enabling integration into a clinical decision support system.

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Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** First principal strain distribution in an L1 vertebra for different lytic tumour scenarios obtained using the automated modelling approach: (a) healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, and (d) $R = 15.9$ mm. **Figure S2:** Third principal strain distribution in an L1 vertebra for different lytic tumour scenarios obtained using the automated modelling approach: (a) healthy vertebra, (b) $R = 3.2$ mm, (c) $R = 9.5$ mm, and (d) $R = 15.9$ mm.