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B. Kozlíková, M. Krone, and N. N. Smit (Editors)

Uncertainty-aware Brain Lesion Visualization

Christina Gillmann[1], Dorothee Saur[2], Thomas Wischgoll[3], Karl−Titus Hoffmann[2],
Hans Hagen[4], Ross Maciejewski[5] and Gerik Scheuermann[1]

[1]Leipzig University, Germany
[2]Leipzig University, Medical Centre, Germany
[3] Wright State University, U.S.A.
[4] University of Kaiserslautern, Germany
[5] Arizona State University, U.S.A.

Abstract

A brain lesion is an area of tissue that has been damaged through injury or disease. Its analysis is an essential task for medical researchers to understand diseases and find proper treatments. In this context, visualization approaches became an important tool to locate, quantify, and analyze brain lesions. Unfortunately, image uncertainty highly effects the accuracy of the visualization output. These effects are not covered well in existing approaches, leading to miss-interpretation or a lack of trust in the analysis result. In this work, we present an uncertainty-aware visualization pipeline especially designed for brain lesions. Our method is based on an uncertainty measure for image data that forms the input of an uncertainty-aware segmentation approach. Here, medical doctors can determine the lesion in the patient's brain and the result can be visualized by an uncertainty-aware geometry rendering. We applied our approach to two patient datasets to review the lesions. Our results indicate increased knowledge discovery in brain lesion analysis that provides a quantification of trust in the generated results.
Keywords: Medical Visualization, Uncertainty Visualization, Brain Lesion Visualization

1. Introduction

A lesion is an area of tissue that has been damaged through injury or disease [BGZL00]. Lesions can occur in any type of tissue. In this case, we focus on brain lesions. A precise detection of brain lesions is of particular importance for diagnosis and prognosis of the underlying disease. Major causes include tumors, inflammation or ischemia [ABH*09]. In many cases, lesions are hard to discern from the surrounding tissue, even for medical experts. They can shrink or grow depending on the patient's condition and their origin, while appearance can differ depending on the state of disease. Medical researchers acquire images using CT (Computed Tomography) or MRI (Magnetic Resonance Imaging) and review these images in order to derive a decision on how to treat the patient. Advanced visualization techniques hold a high potential to localize lesions, examine their size and shape, and/or analyze their impact to the surrounding tissue [CHYD18]. Still, they are barely used. In many instances lesions can be hard to quantify exactly in medical images resulting from an inhomogeneity of the lesioned tissues and a variety of image artifacts such as image resolution, object motion, partial volume effects, or pixel/voxel bleeding [BGZL00]. When examining lesions with traditional visualization techniques the uncertainty captured in the image is not communicated in the computational result, which leads to a lack of trust by clinicians using novel visualization approaches. Clinicians are responsible for the decisions they are making; therefore, they require information on the uncertainty inherent in the post-processing results. Although uncertainty in image data can dramatically influence the decision-making process [SSK*16], a suitable approach to handle uncertainty in brain lesion visualization is not available, as shown in Section 2 for brain lesion analysis.
This raises the need for a novel visualization approach that allows clinicians to review brain lesion data while providing an awareness of the uncertainty of the presented visualization. In this paper, we present a visualization approach that allows to review brain lesion data and reflect the uncertainty captured in the dataset, as shown in Section 3. Here, we provide an uncertainty measure that can be applied to the input dataset. Based on this, medical researchers are enabled to perform an uncertainty-aware segmentation approach in order to localize the lesion in a brain. At last, we allow an uncertainty-aware geometry visualization of the lesion surface that indicates the potential variance in the appearance of the brain lesion.

In summary, this paper contributes:

- Uncertainty quantification of brain lesion imaging
- Uncertainty-aware visualization of brain lesion imaging

This manuscript is the result of a close collaboration between visualization, medical researchers, and neurology researchers. The applicability of our proposed visualization is shown by applying the pipeline to two different real-world medical cases (Section 4).

We then provide user feedback about the benefits and weaknesses of the proposed pipeline. Results are discussed in Section 4.2.

2. Related Work

In this section we summarize previous work in the area of uncertainty-aware visualization of brain lesion imaging.

Image segmentation approaches and their visualization using a fuzzy segmentation result for uncertainty is wide-spread class of methods and a broad overview is summarized by Naz at al. [NMI10]. Lelandais et al. [LGM*14] stated that users need to explore a segmentation result that is affected by uncertainty in order to assist in the decision process. Puig and Raidou [FMW*18] showed how to explore image uncertainty in segmentation results using a workflow that assists users in exploring the uncertainty of segmentation results. Teelen [Tee10] provided an uncertainty-aware geometric description that allows moving points in space. This method was extended by Drapikowski [Dra08] by quantifying and visualizing the uncertainty of surfaces. These methods allow the user to transform an input image that is affected by uncertainty into a into a geometric representation, but they need to be adapted to be applied in brain lesion visualization.

Available image processing and visualization pipeline approaches are highly specialized and available for neuroimaging [vMSKN18] in general. A generalized version for medical image processing was given by Ritter et al. [RBH*11]. Here, uncertainty-aware visualizations are required. An overview of uncertainty-aware visualization can be found by Potter et al. [PRJ12]. Although this provides an overview over uncertainty-aware visualizations, the work does not show how an uncertainty-aware image processing pipeline can be composed. In our work, we carefully select suitable approaches that help users understand the uncertainty of the input image as well as the computational results.

Crinion et al. [CRI] acknowledged the effect of uncertainty in the brain lesion analysis process. In their work, they aimed to quantify the input uncertainty of the considered image data. This is a good starting point for uncertainty analysis in image processing, but they did not consider a propagation of the input images' uncertainty throughout the applied image processing pipeline.
Gillmann et al. [GMP*18] presented an uncertainty-aware workflow for keyhole surgery planning. Although not directly considered with brain lesion analysis, the approach provides an extensive analysis of image uncertainty and provides mechanism that propagate uncertainty throughout each computational step in the image processing pipeline. In this work, we will follow this paradigm and transfer it to brain lesion analysis.

3. Methods

In order to provide a suitable uncertainty-aware visualization for brain lesions, we need to identify the lesion in the patient's brain and determine a proper visualization. As medical image data is usually affected by uncertainty, this uncertainty needs to be quantified.

Here, we utilize selected algorithms to achieve a proper visualization. The selected algorithms had to fulfill two requirements: Each algorithm needs to be able to propagate uncertainty throughout its computation and the algorithms needs to provide a suitable visual paradigm to communicate the uncertainty of the computational output. The overall pipeline consists of three steps: Uncertainty quantification of the input image (see Section 3.1), uncertainty-aware image segmentation (see Section 3.2), and uncertainty-aware visualization of brain lesions (see Section 3.3). These steps will be explained in the following.

In order to achieve a unified nomenclature, the following definitions will be made. Let I_z be an input image containing z voxels in total, where each voxel contains a intensity value d. $I(v)$ outputs the intensity value of pixel v, $N(v,k)$ returns the pixels in k 8-distance to pixel v, and I_r outputs the range of allowed pixel/voxel values.

3.1. Uncertainty Quantification of Input Image

Contrary to an image error that can be measured and precisely quantified, a unique definition for the term uncertainty does not exist. This is due to the different types of uncertainty that can originate from the lack of precision in a computational model or physical effects when acquiring the image. As lesion examination can be performed by different imaging techniques and their combination, a unique definition of uncertainty in medical images cannot be achieved. We presented a variety of uncertainty measures to our medical collaborators where they declared that the selected ones fit their needs and the physics of the captured images best. Here, two measures where selected, as shown in the following.

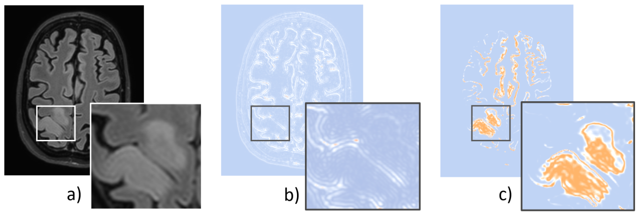

Figure 1: *Uncertainty measures for brain lesion using a color scale ranging from blue (no uncertainty) over white to orange (high uncertainty). a) MRI containing a brain tumor as shown in the closeup. b) Artifact uncertainty. c) Threshold uncertainty.*

Artifact-based Uncertainty can be described by a salt-and-pepper estimation [Alq18]. If a voxel varies too strongly from its surrounding area, it is likely that it shows a salt-and-pepper error. The uncertainty of an image pixel v based on a salt-and-pepper error can be computed by:

$$u_A(v,k) = \left| \frac{\sum_{w \in N(v,k)} I(w)}{|N(v,k)|} - I(v) \right| \div I_r \quad (1)$$

The *Threshold-based Uncertainty* originates from the fact that clinicians often generate parameter maps that are built based on the input images. Here, certain thresholds are applied to classify voxels that represent a specific behavior. The applied thresholds are based on a variety of experiments and are trustworthy to a certain extent, but their exact value cannot be determined precisely due to incomplete knowledge. Here, we offer a threshold-based uncertainty measure. The closer an intensity value in an image is to the threshold, the higher its uncertainty. Here, clinicians are able to choose

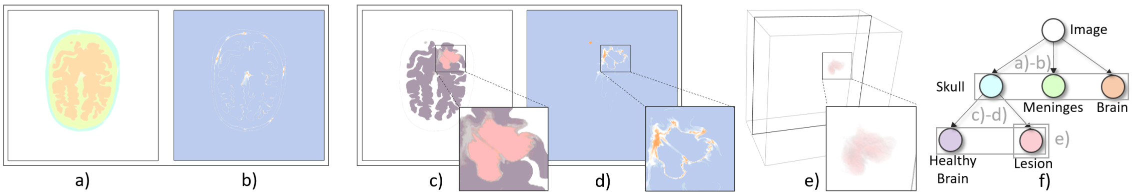

Figure 2: *Uncertainty-aware image segmentation of the input image shown in Figure 1. a) The image is separated into background (white), skull (blue), meninges (green) and brain (orange). b) Uncertainty of the resulting segmentation in a). c) Re-segmentation of the brain into healthy tissue (purple) and lesion (pink). d) Uncertainty of the resulting segmentation in c). c)-d) hold a closeup of the visualization that show uncertain areas of the segmentation result. e) Volume rendering of segmented lesion. f) Segmentation tree of hierarchical segmentation.*

a density value d present in the original image and they can define a σ that describes the standard deviation of the chosen value. The *threshold-based uncertainty* can be computed as follows:

$$u_T(I(v)) = -\frac{1}{\sqrt{2\pi\sigma}} * e^{\frac{(I(v)-d)^2}{2\sigma^2}} \tag{2}$$

Figure 1 shows the results of the presented uncertainty measures. To visualize the uncertainty in each pixel, we selected a color scheme that ranges from blues (no uncertainty) over white (intermediate uncertainty) to orange (highest uncertainty). The results show a closeup of the area that contains the tumor of the patient. Figure 1 b) shows the result of the salt-and-pepper uncertainty measure $u_A(I)$ according to the input image in Figure 1 a). Here, most pixels seem to be certain except for border pixels where intermediate and high uncertainty occurs. Figure 1 d) shows the result of the threshold-based uncertainty when utilizing $d = 115$ and a $\sigma = 7.0$. Together, the image and its uncertainty quantification form an uncertainty-aware image defined as a tuple $\hat{I} = (I, U(I))$, which can be reviewed side-by-side. The images and their uncertainty can form an input for our visualization pipeline.

3.2. Uncertainty-aware Image Segmentation

Image segmentation is an important task in brain lesion visualization to determine which part of the image shows the lesion [SBV*93]. Due to a lack of crisp boundaries in brain imaging, an uncertainty-aware segmentation approach is a desired feature.

The presented work-flow contains a semi-automatic segmentation algorithm that is specifically designed for bio-medical purposes. Users are enabled to create arbitrary segmentation trees capturing the desired segmentation classes. Here, clinicians can encode their mental model of how objects are composed of different substructures [Web02]. The segmentation tree can be redefined to an arbitrary degree meaning classes can be separated further. Clinicians can insert their knowledge into the segmentation process by selecting seed points that are used as a computational basis for the underlying algorithm and classes can be designed freely, depending on the present lesion(s) in the underlying dataset. The algorithm is able to utilize an uncertainty quantification as an input of the image that needs to be segmented. Uncertain pixels will be considered in the segmentation process. The segmentation result is computed based on a geodesic distance according to the selected seed points. Pixels that are similar according to the geodesic distance will gain a high probability to be contained in the respective class. The segmentation result can be redefined and is guided by an uncertainty-aware visualization that indicates areas which cannot be separated according to the given user input. As opposed to classical segmentation approaches, where each pixel is classified as being part of one of the defined classes, we are able to output a probabilistic segmentation result based on the underlying image uncertainty [GPW*19]. Figure 2 shows the segmentation result when considering the brain lesion shown in Figure 1 a). Although the segmentation was computed in 3D, we show an example 2D slice as a result to avoid spatial occlusion. Figure 2 a) shows the first segmentation level of the brain into background (white), skull (blue), meninges (green), and brain (orange). Figure 2 b) shows the uncertainty resulting in the segmentation process. In this example, especially the boundaries between the different structures turn out to be uncertain. In a next step (see Figure 2 c), the brain of the patient is segmented into healthy brain and lesion, but a clear boundary between the healthy tissue and the lesion cannot be determined. Instead the algorithm indicates uncertain areas as light uncolored areas. In addition, the resulting uncertainty can be reviewed indicating the strength of uncertainty while trying to divide pixels into the different classes. The resulting segmentation tree can be reviewed in Figure 2 f).

3.3. Uncertainty-aware Visualization of Brain Lesion

The presented visualization is based on an uncertainty-aware description of geometric primitives. Here, points are not at a fixed position in space. Instead, a probabilistic distribution function describes the probability of a point for each location in the 3D space:

$$N_{\mu,\Sigma}(P) = \frac{1}{\sqrt{(2\pi)^3 \dot{d}et(\Sigma)}} e^{-\frac{1}{2}(P-\mu)^T \Sigma^{-1}(P-\mu)} \tag{3}$$

These functions need to be defined for each point. In the presented setup Σ is the extracted point from the image. These points are acquired by performing a marching cubes algorithm [LC87]. In general, every geometry extraction algorithm can be utilized to generate these points. In addition, μ can be defined as the uncertainty $U^*(I)$, when probing and interpolating the uncertainty image $U(I)$.

In order to present this uncertainty to clinicians, the proposed visualization contains an uncertainty-aware representation for geometric objects [GWHA18]. Geometric representations are extended

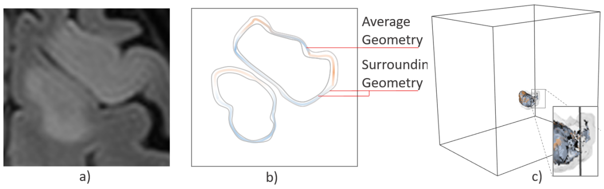

Figure 3: *Geometry extraction of lesion boundary from the segmented image data. a) Closeup of tumor that needs to be extracted. b) Uncertainty-aware boundary extraction of tumor closeup. The center line represents the average appearance of the tumor boundary with a color coding representing the uncertainty of the tumor point. The surrounding surfaces represent the spatial uncertainty of the boundary points. c) 3D extracted geometry of tumor.*

to capture the positional uncertainty of the extracted geometries. The methodology utilizes a classic isosurface to show the most likely appearance of the selected structure, while providing a color coding of the uncertainty captured in each surface point (blue low, white medium, orange high). Further isosurfaces that indicate the positional uncertainty of the extracted geometry are shown by transparent isosurfaces. This surface is generated by sampling the space around the uncertainty-aware points. For each sampled point in space the probability that a point of the surface geometry is located at the sampled point will be computed. At last, the sampled grid can be used as an input for marching cubes. The output surface describes a hull containing all possible surface geometries with a probability p that is used as the isovalue.
Figure 3 shows an uncertainty-aware visualization of a brain tumor where 3 a) recaps the original image as a closeup of the tumor. Figure 3 b) shows an isosurface extraction of the boundary of the tumor. Here, the center line of the representation shows the extracted surface from the marching cubes algorithm. The line is color-coded to indicate the uncertainty probed in each individual line point. Furthermore, the color-coded line is surrounded by a surrounding geometry that indicates the spatial displacement of the boundary points for a probability of 99%.

4. Results and Discussion

This section shows the applicability of the presented uncertainty-aware visualization of brain lesion and discuss the results.

4.1. Results

Brain Tumor Analysis. The first use-case is a brain tumor detection. This example was used throughout Section 3 to demonstrate the presented image processing and visualization approaches.
The image data utilized was retrieved as an MRI scan holding a size of $336 \times 336 \times 326$ pixels. In the image, a patient's head is covered where the brain is affected by a tumor. It is important for clinicians to know how large the tumor can be, where it is located, and what therapy options can be pursued.
In the presented case, we first applied a suitable uncertainty-quantification as shown in 1 b). The clinicians where especially interested in the pixels that hold a high salt and pepper uncertainty (40%) as well as pixels that contain a value higher then 120 (60%). This threshold was chosen to map the clinicians' impression of which values are present in the tumor.

As a first step, a segmentation approach was applied. After dividing the brain from the meninges, the scull and the background, the brain was further separated into healthy and damaged tissue. Figure 2 c) shows the segmentation result where parts of the border cannot be determined clearly. This can also be seen in the uncertainty visualization of the segmentation result (Figure 2 d)). Here, pixels around the tumor are highlighted in white and even orange to indicate a medium and high uncertainty in the segmentation result. To obtain a detailed impression as to how the tumors border could vary, a geometry extraction based on the segmentation result was applied. The threshold for surface extraction was set to 90%, which means that only pixels that are identified with more than 90% probability as representing tumor tissue were considered in the surface extraction. To encode the uncertainty of the selection of the isosurface the uncertainty of the segmentation result was combined with the uncertainty of the thresholding image operation. Based on this threshold, the computation of the surrounding surfaces was possible, as shown in Figure 3 b) (2D) and c) (3D).
This example shows how easy clinicians can review their datasets while using the provided visualization mechanisms. The slice-by-slice based visualization approaches that are embedded in a three-dimensional context allowed a use of the presented approach without requiring a long learning process. In addition, the visualizations are able to quickly highlight steps in the image processing pipeline that output non-optimal results.

Stroke Lesion Detection. In this example we consider a brain lesions caused by insufficient blood supply during a stroke. We considered an MRI with a size of $336 \times 336 \times 326$ pixels. First, the artifact based uncertainty-quantification was applied.
Then, the segmentation was performed. The input image was segmented into patient and background. The head of the patient is divided into skull, meninges and brain. In the brain, the lesion was separated from the healthy brain. The resulting segmentation tree can be reviewed in Figure 4 a), and a volume rendering can be found in Figure 4 b).
At last, the segmentation of the lesion was used as an input in for an uncertainty-aware visualization. We combined the uncertainty of the segmentation output with the threshold uncertainty for a threshold of 90% of the maximum value captured in the segmentation result. The resulting uncertainty-aware geometry extraction is shown in Figure 4 c). This example shows how the uncertainty-aware image processing pipeline helps clinicians to apply various image processing approaches while reviewing the effects of each to the underlying image uncertainty.

4.2. Discussion

Improvements in Brain Lesion Analysis. As the results show, the presented approach allows clinicians to explore and examine brain lesion datasets in an effective manner while tracing the input images uncertainty. We chose visualization approaches that are based on the slice-by-slice reviewing technique which makes it easy for clinicians to use the provided image segmentation approach and show an uncertainty-aware visualization

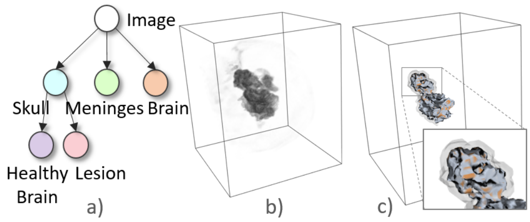

Figure 4: *Uncertainty-aware brain lesion analysis of stroke. a) Segmentation tree. b) Volume rendering of segmented lesion. c) Uncertainty-aware geometry extraction of lesion.*

Furthermore, we provided meaningful visualization approaches in form of an extended slice-by-slice approach which is embedded in a three-dimensional context. Considering the interactivity of the presented system, we allow a variety of image operations, which can be manipulated through useful parameters that are well known in brain lesion visualization.

Expert Feedback. Our medical collaborators were satisfied by the chosen visual variables that communicate the uncertainty of each computational step. Especially the incorporation in the slice-by-slice reviewing technique made it very easy for them to understand the expressed uncertainty. They liked the selection of image processing techniques as it provided them with a variety of tools that are required for brain lesion visualization. For future work, they wish for further techniques like image registration and normalization approaches. This is possible due to the flexible design of the presented visualization pipeline.

5. Conclusion and Future Work

In this paper we presented an uncertainty-aware visualization of brain lesion data. The visualization pipeline includes a proper quantification of the input data, an uncertainty-aware segmentation approach and an uncertainty-aware geometry representation of the identified lesion.

We showed the effectiveness of the presented pipeline by applying it to two real world datasets.. This work is based on a vivid collaboration between clinicians and visualization researchers that allowed us to design and refine each step in the presented pipeline according to our user's needs. As future work we plan to create and maintain an open source project that implements the presented pipeline for brain lesion visualization. Further image operations, visualization approaches, and interaction methodologies will be added successively in order to provide a flexible pipeline. We aim to tackle more application scenarios and examine further applicability.

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