Hesse Rendering for Computer Aided Visualization and Analysis (CAVA) of Anomalies in Chest CT and Breast MRI

Rafael Wiemker\textsuperscript{a}, PhD
Ekta D. Dharaiya\textsuperscript{b}, MS
Thomas Bülow\textsuperscript{a}, PhD

\textsuperscript{a} Philips Research Hamburg, Germany
\textsuperscript{b} Philips Healthcare CT, Cleveland, USA

corresponding author:
Rafael Wiemker
Philips Research Hamburg
Röntgenstraße 24
22335 Hamburg, Germany
Tel: +49 40 / 5078 - 2931 Fax +49 40 / 5078 - 2510
E-mail: Rafael.Wiemker@philips.com

Co-authors’ e-mail:
Ekta.Shah@philips.com
Thomas.Buelow@philips.com

Financial disclosure: all authors are employees of Philips
Hesse Rendering for Computer Aided Visualization and Analysis (CAVA) of Anomalies in Chest CT and Breast MRI

Abstract

We investigate a volume rendering technique that applies image enhancement filters to three-dimensional image volumes and visualizes the filter responses in a color-coded fashion. Complementary to the widely used direct volume rendering which relies on intensities, the proposed technique renders shape properties. Thereby, nodular structures automatically yield different colors than tubular structures, and thus stand out in the rendering. The resulting overview renderings are mouse-click sensitive and can be used to navigate to locations of possible anomalies in the original stack of slice images. This technique, with respect to its mathematical foundations called Hesse rendering, is meant to complement rather than to replace conventional slice-wise viewing or volume renderings. Hesse rendering is a pure visualization technique without internal segmentations or explicit object detection. Nevertheless, similarly to computer aided detection, Hesse rendering may be effective for quickly guiding the attention of the interpreting physician to points of interest in large stacks of slice images and to help avoiding oversights.
One-Sentence-Summary

We introduce a volume rendering technique for visualization of possible anomalies in CT and MR images, using color coding of local shape properties instead of intensity values.

Teaching Points

- Similar to direct volume rendering which derives the colors from the grayscale values or densities of an image volume, Hesse rendering derives the colors and opacities from the local shape in a small neighborhood around each voxel.

- This visualization technique can be beneficial for structures which can vary widely in density but are identifiable by shape, e.g. vessels, nodules and lymph nodes.

- First and second derivatives, commonly used for edge detection, can also be utilized for efficient computation of the local surface curvature at every voxel and appropriate color coding.

- Hesse rendering can be used as an effective aid for navigation through a volume image to quickly draw the interpreting physician’s attention to possible anomalies, and can thus be utilized complementary to computer aided detection approaches.

- Hesse rendering uses derivatives which are more prone to noise than original image data; this can be mitigated by smoothing but will lead to slightly reduced spatial resolution.
1. Introduction

Volumetric image data as produced by tomographic modalities such as CT and MRI has the fundamental problem that it cannot be appraised in a single glance such as a two-dimensional image, e.g. an X-ray image. The most common way to present the content of a three-dimensional image volume is as a series of slice images. In the early days of tomographic imaging with only few and thick slices, these slice images could still all be assembled into a single combined print-out, e.g. for hanging onto a light box. With the advent of multi-slice CT scanners and the possibility of producing thin-slice scans of nearly isotropic resolution within seconds, this is no longer possible. Instead, softcopy viewing with interactive scrolling through the slice images is commonly used to review the three-dimensional image information.

Complementary to slice-wise viewing, there is also the option of making projection renderings. The concept of projection means that the three-dimensional image volume is projected along a certain viewing direction onto a two-dimensional projection image or rendering. The most familiar projection types are maximum intensity projections (MIP), minimum intensity projections (MinIP), and digitally reconstructed radiographs (DRR), which are mapping the maximum value, the minimum value, or a certain physically motivated accumulation function, respectively, along each view ray traversing the image volume (1)(2).

Whereas an image reformat normally refers to a relatively thin slice image cutting through the three-dimensional image volume, a projection comprises the whole image volume or at least a
thick slab. Any projection is of course dependent on the viewing direction, which can be fixed or interactively rotated by the user.

Yet another kind of projection is direct volume rendering (DVR), which emulates a light ray passing through voxels of varying opacity and color. The opacity and, optionally, the color of each voxel is derived directly from its intensity (for CT equivalent to the voxel attenuation or density) by virtue of certain look-up functions (3)(4)(5). Particularly for image volumes of nearly isotropic resolution, DVRs are known to produce impressive renderings of anatomical structures.

Direct volume rendering methods (often abbreviated to volume rendering as opposed to surface rendering) use all image voxels without prior classification or segmentation. In the term direct volume rendering, the word direct aims to distinguish it from other rendering approaches, e.g. surface rendering, which first perform a segmentation of the image volumes to delineate the objects of interest. These segmented objects are then commonly represented as surface triangle meshes, and then shown as surface renderings. This type of rendering is not a direct projection but implies that for each voxel of the overall image volume, an algorithmic decision (labeling) is made designating each voxel to be part of a structure of interest or of the background. Surface renderings of explicit segmentations are known to be more prone to artifacts than the direct projection types, as the latter treat all voxels on equal footing (1).

All projection types discussed above (MIP, MinIP, DRR, DVR) rely entirely on the assumption that the various anatomical structures of interest have different voxel intensities, which for CT correspond to tissue densities. Even though this can successfully discriminate between many tissue types (e.g. muscle, fat, bone), the density alone will in general not
suffice to single out e.g. lung nodules or lymph nodes, firstly because their density can vary widely, and secondly, because the surrounding anatomical structures may have a similar density range. E.g. lung nodules stand out from their surrounding not by their density but rather by their roundish shape.

We therefore want to discuss a type of volume rendering which is not based on voxel values (densities) but rather on local shape properties which can discriminate planar, cylindrical and spherical surfaces. Using these shape properties a color-coding can be applied that assigns different colors to planar, tubular, and nodular anatomical structures, respectively. An example of such a color coding scheme (the choice of colors is arbitrary) is shown in Fig.1, and a resulting rendering in Fig.2:

- planar structures are assigned no color at all (vanishing opacity, i.e. transparent),
- bright tubular structures on a dark background (e.g. vessels) are assigned red color,
- bright nodular structures on dark background (e.g. lung nodules) are assigned yellow color,
- dark tubular structures on bright background (e.g. airways) are assigned blue color.

{TP1: Similar to direct volume rendering which derives the colors from the grayscale values or densities of an image volume, Hesse rendering derives the colors and opacities from the local shape in a small neighborhood around each voxel.}

The main aim we want to achieve is that objects in the foreground do not occlude objects behind them if these have a more relevant shape (in the context of a given application), regardless of their densities. Planar structures should not occlude tubular structures, and tubular structures in turn should not occlude nodular structures.

{TP 2: This visualization technique can be beneficial for structures which can vary widely in density but are identifiable by shape, e.g. vessels, nodules and lymph nodes.}
To determine the local shape properties of a given voxel, the voxel value alone is not sufficient. Instead, a small neighborhood around each voxel has to be sampled. The local shape can then be approximated by virtue of the gradient vector and the Hessian matrix, developed in the 19th century by the German mathematician Ludwig Otto Hesse. More mathematical details will be discussed in the following section. The required mathematical tools, first and second derivatives, are known to be closely related to edge detection and human visual perception (6).

The concept of using first and second derivatives for volume renderings is not new (7)(8)(9). Also local curvature (computed from first and second derivatives) has been used to control the rendering function (10)(11). However, the use has been quite limited so far, and the authors are not aware of previous work where the eigenvalues of the Hessian matrix were used directly for visualization of anomalies. Also, we have to carefully distinguish between approaches which color-code surface curvatures of explicitly segmented surfaces (which has been used to visualize colonic polyps (12)), and direct renderings of implicit surfaces as discussed in this article.

{TP 3: First and second derivatives, commonly used for edge detection, can also be utilized for efficient computation of the local surface curvature at every voxel and appropriate color coding.}

The remainder of this article is organized as follows: In the next section we first explain some underlying mathematical concepts and technical aspects; in the following section we discuss clinical applications of the Hesse rendering; finally, we compare it with computer aided detection and discuss limitations of the method.
2. Mathematical concepts and technical details

In this section we discuss two different conceptual approaches which can be taken to motivate and derive a shape-encoding rendering, from Hessian eigenvalues and from curvature eigenvalues.

Hessian eigenvalues

As stated above, it is important to note that for the rendering discussed in this article we do not use segmented objects. Rather, we propose the direct rendering of the local shape properties of every voxel. To first and second order, the local shape is known to be encoded in the gradient vector and the Hessian matrix, a fact which has been exploited extensively for the detection of vessels, nodules, polyps and airways (12)(13)(14)(15).

The gradient vector is a three-dimensional vector consisting of the first derivatives in three-dimensional space. First derivatives can be thought of as the rate of change of the grayscale values in the direct vicinity of a given voxel position along a given direction. The gradient vector points to the direction of strongest intensity ascent in the grayscale image volume. The magnitude of the gradient vector describes the absolute strength of the intensity change in the vicinity of a given voxel, and is often used for edge detection purposes.

The local Hessian is a $3 \times 3$ matrix and composed of the various combinations of second derivatives in the three-dimensional space. Second derivatives can be thought of as the rate with which the gradient vector changes when the voxel position is varied. E.g. on a planar position, the gradient does not change at all, on a cylinder surface it changes perpendicular to the cylinder axis but not along the cylinder axis, and on a sphere the direction of the gradient...
changes along all directions. The Hesse matrix can be computed for every voxel in the image volume, typically by sampling within a small $5 \times 5 \times 5$ neighborhood around the central voxel. A quadratic matrix such as the Hessian can be advantageously described by its eigenvectors (the non-zero vectors which, after being multiplied by the matrix, remain proportional to the original vector) and the corresponding eigenvalues (the factor by which the eigenvector changes when multiplied by the matrix). Since we are not interested in the orientation of the local shape, but only its type, we do not need to exploit the complete Hessian matrix but only its three eigenvalues. Computation of the eigenvalues is a computationally cheap standard operation.

It is well known that in 3D a plane of homogeneous intensity is signified by one strong and two vanishing eigenvalues of the Hessian matrix, a straight cylinder by two strong and one vanishing eigenvalue, and a sphere by three strong eigenvalues. Because we are not interested in straight planar edges, we can simply disregard the magnitude of the strongest eigenvalue, and consider only its sign, which indicates whether the object is brighter than the background or vice versa. The magnitude of the weaker two eigenvalues can then directly be mapped onto two corresponding color intensities for rendering, e.g. red and yellow, for a negative sign of the strongest eigenvalue, and blue and green, for a positive sign. Since the Hessian eigenvalues are directly mapped onto color intensities, the term Hesse rendering might be appropriate. An example of this rendering scheme for a simulated synthetic image volume is shown in Fig.3.

**Curvature eigenvalues**

For completeness, we would like to discuss an alternative rendering scheme which is based on the concept of surface curvatures instead of second derivatives. The concept of two-dimensional curvature can be intuitively understood as the degree of bending of a two-
dimensional surface embedded in three-dimensional space. If we depict a cylindrical structure such as a vessel as an extended cylindrical body with a certain diameter, then the surface of this vessel cylinder is straight along the principal direction of the vessel, and curved perpendicular to this direction. In contrast, for a spherical structure, the sphere’s surface is curved along both orthogonal directions.

This explanation is based on a solid structure with a clearly defined surface. For a curvature controlled rendering, this would require that the structures such as vessels or nodules are already segmented, before the analysis of their surface could be started. For unsegmented image volumes, we have the concept of the isophote surface, which is the surface implicitly given by two-dimensional layers of equal brightness in a three-dimensional image volume. For illustration, let us consider a spherical structure with a high central intensity which is gradually decreasing and fading into a low intensity background, appearing like a glow on a dark background. Even though this three-dimensional structure has no clearly defined edge anywhere, we can for each intensity value identify a two-dimensional surface of constant intensity around the center of the exemplary sphere. The lower the chosen intensity value is, the larger the surface and the enclosed volume will become. All these so-called isophote surfaces are implicitly defined by the grayscale values in the image volume. For our purpose of characterizing the surface shape, the isophote surface is never explicitly computed, it is only used as a concept to infer the local curvature. For any given point, the isophote surface is normal to the local gradient vector. Therefore it suffices to evaluate the behavior of the gradient vector around the given point to compute the local curvature.

The mathematics of differential geometry teaches that on a two-dimensional surface in a three-dimensional space there are two distinct curvature eigenvalues, which can be computed at every voxel position from the local gradient vector and Hessian matrix. Appropriate
formulae are given in (10). Similar to the Hesse rendering, the two curvature values can be mapped onto two distinct colors for rendering.

**Comparison between Hessian and Curvature eigenvalues**

Mathematically, the Hessian eigenvalues and the curvature eigenvalues are closely related but not equivalent. However, the difference between the rendering results of the two options is not striking (Fig.4). The computational cost is comparable. For reasons of numerical stability one might prefer the Hessian eigenvalues since it is also defined for regions of vanishing gradient.

**Suppression of the blobness filter response at bifurcations**

For the appraisal of Hesse renderings it is important to be aware of the fact that the Hessian eigenvalues at tubular bifurcations or abrupt endpoints of tubular structures can be similar to those on spherical shapes (see Fig.3-5). Technically, it is possible to employ further image processing to suppress this behavior. On the other hand, the interpreting physician may very quickly become accustomed to these manifestations, so that the use of additional processing with its own potentially inherent artifacts should be considered carefully.

**Multi-scale filtering**

The Hesse matrix can be computed with different resolution scales (Fig.6) in order to account for structures of different size. Technically, this is achieved by applying a Gaussian smoothing filter to the image volume before computation of the Hessian eigenvalues (16). One possibility is to compute the Hesse rendering for a fixed resolution scale which is optimal for the structures of interest. Alternatively, the Hesse rendering can benefit from computing several resolution scales, and then taking for each voxel the maximum response of all scales, or a linear combination of the responses.
Projections

Maximum intensity projections (MIPs) and direct volume renderings (DVR) may both be considered as subtypes of a general projection of a three-dimensional image volume onto a two-dimensional rendering image (1). Every projection scheme requires that the values encountered along a view ray of a given direction traversing the image volume are combined into a single grayscale or color value (5). Both projection schemes, MIP and DVR, can be extended to Hesse rendering. Fig.7 shows a direct volume rendering using Hesse coloring, and Fig.8 shows the two-fold comparison between standard MIP and DVR on the one hand, and Hesse-MIP and Hesse-DVR on the other hand (CT dataset courtesy Utrecht Medical Center (17)).

Even though DVRs may produce more impressive images than MIPs, MIPs might be more appropriate for visualization of anomalies because salient signals are less likely to be occluded by a foreground object. The main disadvantage of MIPs in comparison to volume renderings is that they do not convey any depth information. This disadvantage, however, can be easily mitigated by using rotation of the viewing directions. The eye of the observer readily picks up depth cues by movement with interactive rotation of the rendering.

An important advantage of the maximum intensity projection of the features is that the Hesse filter is not required to yield a high response throughout the entire structure, e.g. a nodule or vessel. It is fully sufficient if a view ray through e.g. a nodule picks up a high filter response at least at one point along the view ray to make it visible in the MIP.

In our implementation, we use one MIP for each feature (vessellness, noduleness, airwayness) independently. That is, one MIP is computed for the second Hessian eigenvalue with negative
sign of strongest eigenvalue, another independent MIP for the weakest Hessian eigenvalue with negative sign of strongest eigenvalue, and another MIP for the second Hessian eigenvalue with positive sign of strongest eigenvalue. Additionally, a standard MIP is computed from the grayscale values. These independent four MIPs are finally combined into an overall color MIP, using color coding and simple linear superposition of the individual MIPs. The different weights of the linear combinations can be adapted interactively for optimal perception.

Lung segmentation prior to rendering

Since the Hesse rendering is showing only strongly curved structures while planar surfaces remain translucent, it can indeed be used to render the lung structures without any prior suppression of the thorax surrounding the lung. In contrast, a standard MIP of the whole thorax or a thick coronal slab is not helpful as the lung structures are completely occluded by the surrounding rib cage and thoracic muscle and fat layer. However, even for the Hesse rendering it may sometimes be beneficial to employ a prior lung segmentation and to render only voxels within the segmented lung area. Otherwise the ribs, vertebrae, clothing, infusion tubes and the patient couch may all yield some responses in the rendering and distract from the lung anatomy. It should be noted, however, that an automatic lung segmentation, even though state of the art (18), is not without pitfalls and can sometimes introduce rendering artifacts on the boundaries.
3. Clinical Applications

Use of the Hesse rendering as an aid for image navigation

The Hesse rendering is presented to the interpreting physician in a way to allow interactive rotation of the projection direction, i.e. the viewing angle. In the overall graphical user interface, the Hesse rendering is shown next to a conventional slice viewer. The two viewports are coupled in such a way that a mouse click into the Hesse rendering will automatically select the appropriate slice in the slice viewer and mark the position which contributed most to the clicked-on rendering point (Fig.9). Vice versa, a mouse click into the slice viewer will mark the position in the Hesse rendering where the color values from the clicked-on volume location would appear. This coupling of the two viewports is important, since the idea is not to use the Hesse rendering for diagnostic purposes, but rather as an effective overview to allow quick and effective navigation to locations of possible anomalies. When the interpreting physician has clicked on a possible anomaly in the Hesse rendering, he or she can then inspect the corresponding location in the standard grayscale slice viewer and decide whether further attention is warranted.

{TP 4: Hesse rendering can be used as an effective aid for navigation through a volume image to quickly draw the interpreting physician’s attention to possible anomalies, and can thus be utilized complementary to computer aided detection approaches.}

The term navigation is often used in the context of interventional planning and intraoperative image guided navigation in surgery. It is also used to describe human-computer interaction by means of mouse devices, touch screens, motion, sound, etc. In yet another meaning – the one
referred to in this article – the term *image navigation* is used (19) to describe the user interaction problem of finding anatomical points of interest in three- or higher dimensional image volumes or multiple image datasets. The image navigation aspect is a rather crucial application extension of the visualization technique suggested in this article. The Hesse rendering alone may be an interesting visualization in itself, but a possible improvement of the clinical reading workflow can be facilitated only by coupling the rendering with the standard grayscale slice images.

It has to be noted that the coupling between a two-dimensional point in the rendering and a three-dimensional voxel location in the slice viewer is not unique, because all voxels along a certain view ray could be contributing to the rendering color value. We have mitigated this ambiguity by setting the location to the voxel which contributed most significantly to a certain rendering color value.

**Hesse rendering for lung nodules**

Pulmonary nodules may be an indication for primary lung cancer or metastases from other cancers, and are routinely checked for in CT scans of the chest (20). The rate of missed nodules is known to be substantial (21).

We have applied the Hesse rendering to non-contrast thoracic CT scans which were collected as a ground truth database for pulmonary nodules. Figures 2 and 7-9 show examples to illustrate that pulmonary nodules stand out very clearly in Hesse renderings of the lungs. In particular they are not occluded by surrounding vasculature of approximately the same density (Hounsfield value). Using an interactive rotation of the rendering e.g. around the cranio-caudal axis, the interpreting physician can get a quick overview of the lungs and check the rendering for possible points of interest. Certainly not every yellowish spot indicates a
nodule, but based on clinical experience and anatomical context the radiologist may learn quickly which cues to ignore.

Figure 8 compares four different rendering modes for the projection of a 10 cm thick coronal slab. The standard MIP and DVR can only be meaningfully applied to a slab rather than to the whole lung, since the lung walls would otherwise completely occlude the lung structures. Even using a slab, a substantial part of the internal structure is already occluded in the MIP.

In contrast, the Hesse rendering is much less affected by the lung walls and the nodules are significantly more pronounced due to the color coding. It can also be noticed that the Hesse-DVR yields a better depth perception on the one hand, but that foreground objects may occlude background objects of the same shape.

In addition to a rendering of the whole lung, the principle of Hesse rendering also lends itself readily for application to a singled out nodule. For this purpose, a restricted volume of interest can be selected interactively. Then the rendering is computed for this volume of interest only (Fig.10). For a restricted volume of interest, Hesse-DVR may be more informative than Hesse-MIP. The resulting rendering shows the roundish parts of the nodule in yellow and thus conveys an impression of the three-dimensional size and shape of the nodule. For nodules close to the peripheral lung wall or mediastinum, a standard grayscale MIP or DVR rotated around the nodule would for many viewing directions be occluded by the lung wall, so that the nodule itself would not be discernable. In contrast, the Hesse rendering will show the nodule also if close to a lung wall, since the wall itself has only a negligible curvature and thus becomes transparent to the Hesse rendering.

Let us note again that the rendering is achieved without using any discrete segmentation of the nodule, which for every image voxel would make a binary decision whether it is part of
the nodule or not. Consequently, a volume measure of the nodule can of course not be given by the rendering technique. On the other hand, also the well known pitfalls and ambiguities of discrete segmentation algorithms are avoided, and the interpreting physician is not mislead by erroneous segmentations.

The rendering may also be favorable to appraise the vascular network surrounding the nodule. Using the maximum intensity projection principle for each of the Hesse features (cylindrical, spherical) individually ensures that in a rotating rendering the vessels are not occluded by the nodule body, but stay visible throughout the rotation cycle in a different color than the nodule body. This conveys an improved visual impression of the vascular network surrounding a given nodule, and may aid in the diagnostic and physiological assessment. Note again, that the rendering of the vessels does not rely on a previous discrete segmentation of the vessels, and thus may be less prone to artifacts.

Since the Hesse rendering is only a special visualization, its performance cannot easily be measured using statistical methods as e.g. sensitivity and specificity which are commonly used to evaluate CADe methods. As the new approach does not generate explicit markers it is not possible to specify true or false positives and negatives. Instead, a multi-observer perception study would be required, similar to studies which compare MIP and DVR for the detection of nodules (22). As a surrogate for a clinical observer study, we performed a retrospective analysis on 598 consecutive CT scans from the multi-observer LIDC-IDRI lung nodule database (23)(24). Each thoracic CT scan in the LIDC database has been exhaustively searched by four expert readers for the presence of lung nodules, and nodules with a diameter between 2 and 20 mm were marked. Moreover, for each nodule with a diameter of 3 mm or more its extent was manually delineated. Consensus between the expert readers was not enforced, so that a nodule can be marked by one, two, three or four readers. Principal
contributors of the CT images and annotations are U Iowa, U Michigan, Cornell U, U Chicago, and UC Los Angeles. For our analysis we have used a total of 1438 delineated nodules (on average 2.4 nodules per scan, and 2.4 observer marks per nodule).

Using the expert-drawn delineations of pulmonary nodules, we compared the enhancement ratio of the Hesse renderings at the locations of the marked nodules with respect to the overall lung area. In that way, we certainly cannot evaluate the overall usefulness of the rendering. However, this measure of contrast between nodules and lung background can give us an indication about the effectiveness of the Hesse rendering in general.

Figure 11 shows the contrast ratio between view rays through nodules and view rays through background as a function of the number of readers who have agreed upon a nodule. We observe that the contrast ratio of nodules vs. background correlates well with the number of readers. In other words, if a nodule is confirmed by more experts, it appears brighter in the Hesse rendering. This indicates the promising potential of the Hesse rendering as an image navigation aid to identify possible anomalies and its accordance with medical expertise.

As a side-benefit, the study allows us to perform a technical comparison of several possible more advanced combinations of the Hessian eigenvalues (25), instead of mapping them directly onto color intensities. In fact, the study may indicate that a certain combination of eigenvalues (13) could be even more effective than a linear mapping of only the weakest Hessian eigenvalue onto the intensity of the, say, yellow color channel.
Hesse rendering for breast lymph nodules

Breast MR imaging shows potential in image based staging of axillary lymph nodes (26). Locating axillary lymph nodes in Breast MR images currently is a tedious process that requires scrolling through the stack of image slices. In standard MIP projections axillary lymph nodes will typically be obscured by other tissue.

We have applied the Hesse rendering to T1-weighted dynamic contrast enhanced breast MR series. For the Hesse rendering, only one of the image volumes of the time series was selected (MRI dataset courtesy University of Chicago (27)).

Figures 12-14 show exemplary that the lymph nodes are enhanced very well in the Hesse rendering, so that also inexperienced readers can very quickly find the principal lymph nodes and can on mouse click navigate to the appropriate location in the standard grayscale slice viewer for closer inspection (Fig.13). We have anecdotal evidence that the lymph enhancing rendering can also lead to incidental findings in regions where the lymph nodes had presumably been resected.
4. Discussion

Computer Aided Visualization & Analysis (CAVA) as an alternative to CADe

The use of the Hesse rendering as an image navigation aid can be seen on a more general background of Computer Aided Visualization & Analysis (CAVA) (28), a paradigm which aims to provide enhanced visualization of medical data in a way as to optimally support diagnoses without anticipating any explicit decision.

The concept of image enhancement (reinforcement of certain structures of interest by application of image filters) is well known, and often used as a pre-processing step for computer aided detection (CADe) schemes (13)(29)(30)(31)(32)(33). CADe algorithms work by going through the entire image volume, computing numerical features, assembling suspicious image regions into discrete objects, segmenting these objects, testing hypothesis about these objects or submitting them to classifiers, and finally compiling a list of possible anomalies and their locations and extent (34)(35). This list of objects is then communicated to the interpreting physician by overlaying graphical markers such as arrows or circles onto the images slices, or by providing a list which can be interactively stepped through.

The paradigm of Computer Aided Detection (CADe), however, has sometimes been received with a certain guardedness in radiological practice because explicit graphical markers such as arrows or circles may be felt to clutter the original image and distract the reader, especially if there is a non negligible false positive rate. Therefore we would like to re-discuss the possibility of using known image enhancement filters in conjunction with color-coded rendering as a possible alternative to classical CADe approaches. In fact, many successful CADe algorithms for lung nodules rely on second derivative filters which respond to roundish
blob-like shapes (13). Three-dimensional image filters are applied to the whole image volume and compute certain local properties for all voxels independently. Since second-derivative based image filters have proven to be essential input for CADe classifiers (13), it may also be considered to visualize their filter responses directly and show this to the interpreting physician.

Instead of showing explicit classification and graphical markers, we aim to exploit the whole color space (intensity, hue, saturation) to combine e.g. various differential geometric properties of an image volume to a blended color and to intuitively convey this information to the reader. In particular we aim to avoid the use of internal object lists of anomaly candidates, of internal segmentations of objects, and of using classifiers to make explicit internal decisions, since all these subsequent steps can be prone to errors which are then propagated in a very non-linear way. Instead, we aim to visualize the relevant information on a strictly voxel-wise basis, and leave the cognitive part to the human reader. The underlying idea is that the human brain seems to be very adaptive in learning which visual cues and patterns are meaningful and which can be ignored. The rendering of sophisticated local image features is not supposed to replace but rather to complement the standard grayscale data, combined with a navigational aid that relates each point in the rendering to its origin in the three-dimensional input image volume.

Since the Hesse rendering is only a special visualization, its performance cannot easily be measured using statistical methods normally applied to CADe. As the new approach does not generate explicit markers it is not possible to specify true or false positives or negatives, or to perform a Free Response Receiver Operating Characteristic (FROC) analysis (36), as is the standard to evaluate and compare CADe algorithms. A comparison between CADe and
CAVA approaches cannot be drawn on a purely software-technical basis, but would require a clinical multi-observer study evaluating the overall man-machine system.

**Limitations and challenges**

Having reviewed the advantages of the Hesse rendering, it might be asked why the technique is not yet in widespread use, even though all necessary ingredients are well known. The inhibiting factors can be divided in technical, clinical, and workflow categories.

The visualization technique as described can only be applied to thin-slice CT or MR datasets, as otherwise the three-dimensional derivatives are not meaningful. Technically, the curvature-based rendering is much more cost intensive than standard direct volume rendering (DVR), demanding more memory as well as more computation time. Standard DVR does not need any data besides the grayscale voxel values of the image volume itself. For Hesse rendering on the other hand, the second derivatives have to be computed from the original grayscale data, this has to be carried out on several resolution scales, and the maximum intensity projection has to be performed for each of the Hesse features separately. If an interactive solution is provided to the interpreting physician, then all these ancillary data volumes have to be kept in the computer memory, and projections have to be re-composed in interactive time. These memory and computation power requirements have been met by standard workstation hardware only recently. The CAVA scheme in general is ideally suited for massively parallel implementations on graphical processing units (GPUs), as all voxels and resolution scales can be treated independently of each other.

As another technical factor, it is well known that derivatives are more prone to noise than the original image data. Subtle artifacts which are barely visible in the original image (which of
course is in itself the result of a specific reconstruction algorithm), may distort higher
derivatives. The noise issue can be mitigated by using higher levels of the resolution scale
space, but only at the cost of losing spatial resolution, thus producing renderings which appear
less sharp than the original image data.

{TP5: Hesse rendering uses derivatives which are more prone to noise than original image
data; this can be mitigated by smoothing but will lead to slightly reduced spatial resolution.}

The inhibiting factor from a workflow perspective is that the Hesse rendering provides yet
another gadget to be looked at, potentially useful, but possibly asking for even more reading
time and dividing further the attention of the interpreting physician. As a workflow tool,
Hesse rendering can be considered beneficial only if it can be proven to either shorten the
reading time by improved navigation through the three-dimensional image volumes, or to be
an effective safeguard against oversight of anomalies hidden in the maze of central
vasculature.

Finally, from a clinical perspective, the foremost task of the interpreting physician of course is
to make clinical decisions. The color coding of differential geometric properties of the
anatomy described here may produce nice looking images but does not provide quantitative
results nor explicit decision support. On the other hand, a well devised visualization can
sometimes tell more than so many words or numbers (37).
5. Summary

As a complement to standard maximum intensity projection (MIP) and direct volume rendering (DVR), a Hesse rendering maps the local second derivatives or curvatures of structures rather than their intensities. Color coding of the local curvatures, or simply of the eigenvalues of the Hessian matrix, can provide an intuitive aid for image navigation to blob-shaped anomalies such as pulmonary nodules and lymph nodes. Preliminary evaluation results based on the LIDC lung image database indicate that the more radiologists agree on a certain anomaly to be a lung nodule, the brighter it appears in the Hesse rendering. The Hesse rendering might thus be an interesting complementary approach to classical computer aided detection with explicit markers.

Acknowledgements

The authors would like to thank the steering committees and industry partners of the Image Database Resource Initiative (IDRI) and the Lung Image Database Consortium (LIDC), in particular Samuel G. Armato III, PhD, (University of Chicago) and Michael Kuhn, PhD, (Philips Healthcare). We are grateful for further CT datasets obtained from Bartjan de Hoop, PhD, and Mathias Prokop, MD, (Utrecht University Medical Center).

Moreover the authors thank Lina Arbash Meinel, PhD, Johannes Buurman, PhD, Liran Goshen, PhD, Peter van Loon, MBA, Cristian Lorenz, PhD, Marcel Quist, PhD, Axel Saalbach, PhD, Jonathan Sapir, MD, Iwo Serlie, PhD, Amnon Steinberg, MS, (Philips Research and Philips Healthcare) as well as Hiroyuki Abe, MD, Gillian Newstead, MD, Robert Schmidt, MD, (University of Chicago) for fruitful discussions and image materials.

The authors are also grateful to the anonymous reviewers and the editors for their many helpful suggestions.
References


29. Murphy K, Schilham A, Gietema H, Prokop M, van Ginneken B. Automated detection of


Figures captions:

Hessian matrix $H = \begin{bmatrix} g_{xx} & g_{xy} & g_{xz} \\ g_{xy} & g_{yy} & g_{yz} \\ g_{xz} & g_{yz} & g_{zz} \end{bmatrix}$

local $H(x, \sigma)$ computed for every position $x$ and resolution $\sigma$

Eigenvalues ordered by magnitude $|\lambda_0| \geq |\lambda_1| \geq |\lambda_2|$

Standard volume rendering $\rightarrow$ derives colors from Hounsfield densities
Hesse-rendering $\rightarrow$ derives colors from local Hessian eigenvalues or local curvature

Basic types:

- **Planar structures**
  - No isosurface curvature
  - No color (translucent)

- **Tubular structures (vessels or airways)**
  - Isosurface curvature in 1 direction $\rightarrow$ intensity $< |\lambda_1|$ 
  - Red (for negative first Hesse eigenvalue)
  - Blue (for positive first Hesse eigenvalue)

- **Spherical structures (nodules or lymph nodes)**
  - Isosurface curvature in 2 directions $\rightarrow$ intensity $< |\lambda_2|$ 
  - Yellow (for negative first Hesse eigenvalue)

Fig. 1:

The underlying principle of Hesse rendering.
Fig. 2: Example of Hesse rendering applied to a thoracic CT data scan (0.6 × 0.6 × 1.5 mm voxel spacing). Nodular structures show up in yellowish colors, tubular structures in reddish colors, even though their Hounsfield densities are undistinguishable. Prior to the rendering, an automatic segmentation of the lungs from the overall thorax was applied. The rendering inside the lungs, however, does not employ segmentation of vessels and nodules, or explicit computer aided detection algorithm, the coloring is due only to the local curvature of the structures.
Fig. 3

A: Standard direct volume rendering of a synthetic three-dimensional dataset with structures idealizing vessels with bifurcations, a solitary nodule, a nodule with three attached vessels, an isolated tubular structure, a planar wall, and a semi-spherical juxta-pleural nodule.

B: Direct volume rendering with colors derived from local Hessian eigenvalues. The synthetic dataset illustrates that planar structures stay transparent in the Hesse rendering, while cylindrical and spherical structures are color-coded.
Fig.4:
Comparison between rendering of Hessian eigenvalues (A-D) and curvatures eigenvalues (E-H), which are mathematically closely related but not equivalent.
A/E: a central slice image of the synthetic three-dimensional dataset (grayscale values),
B/F: a central slice showing the filter response of the second Hessian eigenvalue vs. first curvature eigenvalue (planar structures yield no response),
C/G: a central slice showing the filter response of the weakest Hessian eigenvalue vs. second curvature eigenvalue,
D/H: a maximum intensity projection (MIP) of the Hessian vs. curvature eigenvalues using the suggested color coding scheme and projecting all slices of the synthetic image volume.
Fig. 5:
Suppression of the filter response at bifurcations.
A: Direct rendering of Hessian eigenvalues leads to responses indicating spherical shape also at bifurcations.
B: More sophisticated local combination of the Hessian eigenvalues on different resolution scales can be employed in order to reduce responses at bifurcations, but might also affect highlighting of actual nodules.
Fig. 6:
Comparison of Hessian filter responses on different scale space resolutions (only second Hessian eigenvalue rendered, third eigenvalue omitted for clarity). The filter resolution can be adapted interactively to match the structures of interest.
A: filter resolution $\sigma = 1$ mm,
B: filter resolution $\sigma = 3$ mm.
Fig. 7:

Direct volume rendering (DVR) with Hesse coloring (with a slight overlay of standard DVR in gray).
Fig. 8:
Comparison of Hesse rendering in conjunction with maximum intensity projection (MIP) versus direct volume rendering.

A: Standard direct volume rendering of a 10 cm thick coronal slab, without prior lung segmentation.
B: Direct volume rendering with Hesse color coding.
C: Maximum intensity projection of the 10 cm thick slab is not useful, because most of the lung area is occluded by the lung walls.
D: Maximum intensity projection of the Hessian eigenvalues. Although no prior lung segmentation was used, non-curved structures do not show up in the rendering, and thus the lung walls do not occlude the view.
The freely rotatable Hesse rendering shows in an intuitive way the locations of possible nodules in a lung. The overview rendering can be used as an image navigation aid such that a mouse-click on any point in the anomaly-enhancing rendering will mark the associated position in the original image volume for further inspection. In the CAVA approach (Computer Aided Analysis & Validation) no internal object lists or object segmentations are used, but all voxels are treated on equal footing. The rendering shows a coronal MIP projection of the third eigenvalue of the local Hessian matrix coded in yellow (nodules), and the second eigenvalue in red (vessels).
Fig.10:
Comparison between standard DVR / MIP and Hesse DVR/MIP for an individual nodule. Note that no explicit segmentation was applied to the nodule.
A: Standard direct volume rendering of a volume of interest (VOI) around a nodule.
B: Direct volume rendering with additional color coding of the local Hessian eigenvalues.
C: Standard maximum intensity projection of the VOI.
D: Maximum intensity projection with additional color coded MIPs of the Hessian eigenvalues.
The effectiveness of various possible combinations of the Hessian eigenvalues for rendering can be compared by virtue of the mean rendering contrast ratio as a function of the inter-observer agreement on a pulmonary nodule. Each contrast curve represents a different combination of eigenvalues (25). Ordinate: The contrast ratio of the maximum response for view rays traversing through a reader-delineated nodule versus view rays traversing entirely through lung background and vessels. Abscissa: The nodule-presence value denotes the number of readers who have identified and agreed on a certain nodule (0: no nodule present in view ray; 4: all 4 readers agreed).
Fig. 12:

A: Standard MIP of a breast MR image volume (T1-weighted, from dynamic series).

B: The corresponding Hesse rendering from the same viewing angle. The Hesse rendering shows the lymph nodes in a much more pronounced way, because the other structures of equal or higher intensity become transparent if they are not curved as strongly as vessels and lymph nodes. Thus, the non-curved structures are not occluding the lymph nodes as in the standard grayscale MIP.
**Fig.13:**
Combined graphical user interface with Hesse rendering of a breast MR image volume, and standard grayscale slice viewers in axial, coronal, and sagittal orientation. The slice viewers are automatically centered on the lymph node which is selected by mouse click in the rotatable Hesse rendering (white circle).
Fig.14:
An example of a lymph-node-like anomaly (white circle) which might have gone unnoticed in a standard slice-wise viewing or MIP due to its unusual caudal position (with respect to the axillary lymph nodes), but stands out prominently in the Hesse rendering.