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A Survey on Multimodal Medical Data Visualization

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Abstract

Multi-modal data of the complex human anatomy contain a wealth of information. To visualize and explore such data, techniques for emphasizing important structures and controlling visibility are essential. Such fused overview visualizations guide physicians to suspicious regions to be analysed in detail, e.g. with slice-based viewing. We give an overview of state of the art in multi-modal medical data visualization techniques. Multi-modal medical data consist of multiple scans of the same subject using various acquisition methods, often combining multiple complimentary types of information. Three-dimensional visualization techniques for multi-modal medical data can be used in diagnosis, treatment planning, doctor–patient communication as well as interdisciplinary communication. Over the years, multiple techniques have been developed in order to cope with the various associated challenges and present the relevant information from multiple sources in an insightful way. We present an overview of these techniques and analyse the specific challenges that arise in multi-modal data visualization and how recent works aimed to solve these, often using smart visibility techniques. We provide a taxonomy of these multi-modal visualization applications based on the modalities used and the visualization techniques employed. Additionally, we identify unsolved problems as potential future research directions.

Keywords: medical imaging, visualization, scientific visualization, visualization, volume visualization, visualization

ACM CCS: Medical Imaging [Visualization], Scientific Visualization [Visualization], Volume Visualization [Visualization], Multimodal Medical Data

1. Introduction

Multi-modal medical datasets consist of multiple scans of the same subject using various acquisition methods. In this way, it is possible to image different tissue characteristics. Several modalities can also be integrated directly into the hardware of a single scanner. Of these hybrid medical imaging techniques, positron emission tomography (PET)/computed tomography (CT) is currently the most widespread. More recently, PET/magnetic resonance (MR) became clinically feasible, and single-photon emission computed tomography (SPECT/CT is also used in clinical practice. The common denominator in the aforementioned hybrid imaging combinations is that the structural modality [CT or MR imaging (MRI)] depicts the anatomy of the patient in high spatial resolution, whereas the nuclear medicine modality (PET or SPECT) depicts functional processes, such as metabolism, in a lower resolution. The overall visualization goal in this case is to accurately localize regions featuring abnormal functional values based on their relation to structural anatomical information. Additionally, it is possible to combine structural information from a scan with functional information from the same scanner, such as combining an anatomical MRI acquisition with functional MRI (fMRI) information. In addition to combinations of functional and anatomical imaging, two anatomical imaging techniques can be combined, such as in the work by Beyer *et al.* [BHWB07]. Since both have a rather high spatial resolution, visualization techniques need to be updated.

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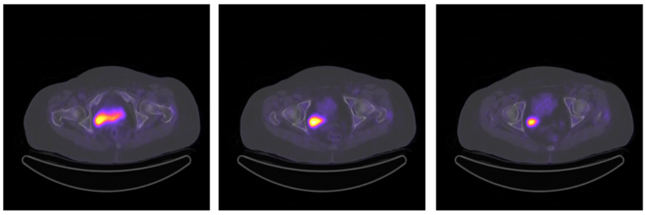


Figure 1: *2D images with superimposed CT and PET data, represented in grey scale and colour, respectively.*

Typically, radiologists or specialists in nuclear medicine examine data in a slice-based fashion consisting of superimposed 2D images with a combined visualization of CT and PET image data, as shown in Figure 1. Here, physicians browse through the slices, setting window and level parameters to adjust the brightness and contrast, and examine structures of interest.

Unfortunately, presenting these 2D images in such a way can hinder full and quick analysis of the data. The physician needs to check every slice, which may be time-consuming as the number of slices increases. Furthermore, physicians need to mentally fuse all information from these slices to form a correct diagnosis. Therefore, visualization techniques that provide a 3D overview are helpful to see potential abnormalities at a glance. This enables the experts to navigate to these suspicious regions for a more detailed exploration in the slice views.

In recent years, the amount of work focusing on multi-modal medical data visualization increased. In 2010, there was an IEEE VIS contest on multi-modal visualization for neurosurgical planning [DPL*11], further highlighting the interest in and importance of multi-modal visualization. With this STAR, we aim to provide a survey of this literature. A number of medical visualization techniques are described in a survey style in the book by Preim and Botha [PB13]. Multi-modal visualization, however, is only slightly touched upon as an add-on to registration, and has not been previously considered in other survey articles. In general, concepts used for visualizing medical data can be extended to other multi-modal visualization application domains, but there are some specific challenges in dealing with medical multi-modal data. Thus, the presented works are of interest to any visualization researcher dealing with multi-modal data. The contributions of this STAR are the following:

- We provide an overview of multi-modal acquisition techniques and relate this to requirements and challenges.
- We propose a taxonomy of multi-modal medical data visualization applications.
- We provide an outlook on open problems in multi-modal medical visualization and a perspective on future research directions.

STAR scope. There have been several surveys on multi-field data visualizations [STS06, FH09]. In contrast to general multi-field data, measured medical image data are not as 'clean' as simulation data, due to the acquisition process, which results in noise. Living tissue is imaged with scanning parameters that favour the patients' safety over image quality, unlike, for instance, applications in material testing. Furthermore, several tasks such as searching for metastases, or assessment of infiltration, are unique to the field, and therefore evaluation of multi-modal medical visualization needs to consider such or similar relevant tasks. While multi-modal medical image data are available at both microscopic and macroscopic level, we focus on the macroscopic level, e.g. radiological image data. We also consider interaction with multi-modal data.

Please note that in this survey, we mainly focus on combining imaging modes acquired by different scanning techniques, and less on combining imaging modes, e.g. MRI T1 and T2, or visualization of original data combined with derived data from a single scanner. A survey focusing on diffusion tensor imaging (DTI) visualization techniques can be found in the recent work by Isenberg [Ise15]. DTI can additionally be used in multi-modal applications when it is combined with fMRI or additional imaging modalities. In contrast to multi-field non-medical data, multi-modal medical data are often acquired from separate scanners, which creates a need for software-based registration to align the volumes. Due to the time between the scans and patient pose differences, it is not straightforward to register multiple volumes accurately. This, in turn, generates additional challenges in dealing with uncertainty in the form of processing errors introduced by the registration process. For an overview of medical image registration, we refer to the survey by Maintz and Viergever [MV98] and more recent work on mutual-information-based registration methods by Pluim *et al.* [PMV03]. A multitude of registration techniques have been developed that can handle multi-modal medical image registration, for instance, methods aimed at multi-modal brain image registration [VMN*01]. In essence, there are many registration techniques that can be employed to align multi-modal datasets, such as maximizing an information-theoretic measure, e.g. normalized cross-correlation and normalized mutual information. These optimization strategies can be costly in terms of processing time, in which case GPU support is necessary [FVW*11].

While blood flow measurements can be considered functional information, a review of these techniques is out of the scope of this survey (see the recent survey on Cardiac 4D PC-MRI [KBvP*15]).

In our survey, we focus on three core applications areas, namely visualizations aimed at research, diagnosis and treatment planning. Within these areas, we distinguish between applications aimed at diagnosis in oncology and cardiology, and applications aimed at treatment planning in neurosurgery and radiotherapy planning.

Paper selection criteria. We searched for papers that were related to multi-modal medical visualization using the EG digital library, where we looked for the following conferences and workshops: EuroVIS, VCBM and VMV in the last 10 years. Furthermore, we used the IEEE digital library and the proceedings of the IEEE VIS conference for the last 10 years. Additionally, we used Google Scholar for finding papers related to our survey, in order to integrate older papers. Specifically, we looked for the following keywords and combinations of these: combined, concurrent, CT, DTI, dual, fMRI, fused, fusion, hybrid, integrated, intermixing, neurosurgery, MRI, multi-field, multi-variate, multi-volume, multi-modal, multiple, PET, planning, simultaneous, SPECT and visualization. We employed 'neurosurgery' as the only application-specific search

Figure 2: *Volume renderings using dual-energy CT scan of an aortic stent. On the left, an overview shows the anatomical context, and on the right, only the aorta and stent are shown. Springer [SH08], ©Springer Medizin Verlag Heidelberg 2008. With permission of Springer.*

term, since this area is the key application for many multi-modal visualization applications so far.

STAR organization. Our survey is structured as follows. In Section 2, we provide an overview of (hybrid) imaging acquisition and what the characteristics, advantages and disadvantages of each of these modalities are. In Section 3, we describe the typical workflow of a specialist in radiology and nuclear medicine for exploration and analysis of the data. Based on this workflow, we derive requirements for 3D visualizations. In Section 4, we provide a brief overview of relevant basic visualization techniques that can be employed in multi-modal visualization. Experienced medical visualization researchers readers may safely skip the basic explanations given in Sections 2 and 4. Section 5 continues with multi-modal rendering and interaction techniques. In Section 6, we focus on applications of multi-modal visualization techniques to real-world clinical data. Section 7 concludes the survey and outlines unsolved problems and challenges for future research. Finally, in Section 8, we conclude with a brief summary.

2. Medical Background

In this section, we provide an overview of multimodal and hybrid imaging, as well as their applications in clinical practice. The characteristics of each of the modalities involved are summarized, and their advantages and disadvantages and associated visualization challenges are discussed.

2.1. Computed tomography

CT is an X-ray-based tomographic imaging technique that creates stacks of 2D cross-sectional images. It is especially suitable to distinguish tissues such as bone, water, fat and the air in the lungs. A contrast agent can be applied to enhance vascular structures. Recently, hybrid scanners such as dual-source or dual-energy CT scanners became available, delivering a final image which fuses information from high- and low-voltage image acquisition performed at the same time (see Figure 2) [KSF11]. Depending on the chosen imaging protocol, this technique allows for differentiation of structures like bone and contrast-enhanced blood vessels.

CT data are especially suited for high-quality direct volume rendering (DVR), due to its high resolution (in general 512×512 in slice resolution and 0.3–2 mm slice thickness), high signal-to-noise ratio and standardized intensity values (Houndsfield Units), allowing the definition of re-usable and task-specific transfer functions.

2.2. Magnetic resonance imaging

In MRI, a scan is made using a powerful magnetic field. In contrast to CT, MRI scanners are highly configurable and provide a large variety of imaging protocols, allowing capture of structural as well as functional information. In general, several different MRI sequences, such as T1 and T2-weighted scans, are acquired at the same time, leading to (more or less) co-registered images. Intensities in MR images are not standardized. MRI data often exhibit an inhomogeneous grey-level distribution, requiring careful pre-processing of the data, and intensity values vary depending on scanner vendor and clinic. Therefore, MRI data are challenging to visualize. Furthermore, due to the unpredictability of the intensity values, transfer functions are not directly applicable across several datasets without dynamic adaptation [RSHSG00]. Finally, MR images have generally a lower resolution and lower signal-to-noise ratio than CT images.

Besides the standard scanning protocols, there are specific MRI sequences and protocols, such as magnetic resonance spectroscopy imaging (MRSI), dynamic contrast-enhanced MRI (DCE-MRI) and diffusion tensor imaging (DTI). In MRSI, spatially localized metabolites in body tissues are measured. DCE-MRI is a perfusion imaging technique that measures the perfusion of tissues by blood, indicating regions damaged by stroke or infarction as well as characterizing the vascularization of tumours, helping to assess whether they are benign [TBB*99]. DTI is an extension of diffusion weighted imaging (DWI), which detects the direction of white matter tracts in the brain, which represent connectivity between different areas of grey matter. DTI is used in clinical practice to assess the deformation of white matter by tumours, for neurosurgical planning and for (early) diagnosis of brain pathologies such as Alzheimer's disease, schizophrenia and multiple scleroses [LBMP*01]. DTI data are often visualized as a scalar field of fractional anisotropy (FA) values, using glyphs or fibre tracking [HS15].

fMRI: fMRI records subtle changes in blood flow in response to stimuli or actions and uses this information to visualize cortical activity. The most frequently employed technique is blood oxygenation-level dependent (BOLD) fMRI. By having the subject perform tasks categorized into visual, motor, speech or memory tasks, different functional areas of the brain 'light up' and can be associated with the tasks performed. Additionally, fMRI is used in a research context to improve the understanding of neural networks in the brain even when the user has no task, as is the case in resting state fMRI [VDHP10].

2.3. Ultrasound

In medical ultrasound, high-frequency sound waves are employed to characterize tissue. Ultrasound can be used for diagnosis, and to guide interventional therapeutic procedures. Due to the nature of the modality, ultrasound is suitable for imaging soft tissues, such as tendons, vessels and organs, but cannot visualize bone and air, or structures lying underneath these tissue types. Based on the Doppler effect, blood flow in the heart and blood vessels can be detected. The advantages of ultrasound compared to other modalities are that it is cheap, safe, portable and real-time. However, ultrasound is difficult to interpret, due to the low signal-to-noise ratio, artefacts and the limited field of view. Recent advances in ultrasound technology include 3D ultrasound [VBS*13], elastography and contrast-enhanced ultrasound using micro-bubbles.

2.4. Modalities from nuclear medicine

PET relies on the indirect detection, via gamma rays emitted from inside the patient, of an administered positron-emitting radionuclide (tracer). While CT and MRI scans can provide detailed anatomical data, PET scans are able to reveal functional information, such as metabolism. A common application of PET scans is to search for metastases, for which the radioactive tracer fluorodeoxyglucose (FDG), a glucose analogue, is used. The metastases have higher glucose uptake than normal, and specific abnormal metabolic activity can be captured in this way. Besides oncological applications, PET is also used for neurological and cardiological diagnostic purposes. While commonly used, FDG is not the only available tracer for PET, and different tracers may be better suited for specific applications [TCV*13].

The PET data need to be attenuation-corrected before visualization. Visualizing PET data in 3D is challenging: since normal metabolic information is also contained in PET, the highest activity measures are not always the most interesting.

SPECT is a nuclear medicine tomographic imaging technique that uses radioactive tracer material to detect gamma rays. In this way, it is similar to PET, but in contrast to PET, gamma radiation is measured directly from the tracer. SPECT is used for oncological diagnosis, but also for infection, thyroid or bone imaging. Besides these applications, SPECT can also provide localized function within organs for functional cardiac or brain imaging. SPECT suffers from a lower spatial resolution and contrast than PET [BW13]. Similar to PET, SPECT data are not straightforward to render in 3D.

2.5. Hybrid scanners

When combining acquisitions from multiple modalities from different scanners, registration problems arise. To avoid the registration process, efforts have been made to integrate multiple modalities into hybrid scanners that combine the best of both worlds in structural and functional imaging. Hybrid imaging scanners combining PET or SPECT with CT are already commonplace in clinical practice, while combining PET or SPECT with MRI is more recent development [Che09] for which the first prototypes have been made [PKNS10]. In a preliminary study comparing clinical impact of PET/CT and PET/MRI, PET/MRI imaging outperformed PET/CT and more frequently affected patient management [CRS*13]. Furthermore, integrated whole-body PET/MRI was found feasible in a clinical setting with comparable reliability to PET/CT for this purpose [DSE*12]. Since 2014 the very first devices are legally allowed and used in clinical practice, focused on head and neck imaging initially.

Figure 3: *A PET/CT scanner developed by Siemens Healthcare. Photo courtesy of the Centre for Nuclear Medicine and PET, Department of Radiology, Haukeland University Hospital in Bergen, Norway.*

PET/CT: While PET, CT and MRI all provide valuable information by themselves, they can be combined to provide more insight into the exact localization of suspicious metabolic activity. By combining PET and CT/MRI scans, physicians are able to detect (abnormal) metabolic activity using the PET scan and to localize this activity using the CT or MRI scan. This can aid the user in distinguishing which activity is physiologically normal and which is pathological. Since the adaptation of PET/CT is more widespread clinically, we focus on this hybrid imaging techniques in the rest of this section (see Figure 3).

CT data are also used to perform noiseless attenuation correction on the PET data, thus eliminating the need for an additional PET transmission scan for this purpose. This can reduce the total scanning time by up to 40% [TCYH04]. A drawback of PET/CT is that the imaging is performed sequentially, which takes more time and eliminates temporal correlation between the modalities [JWN*08].

Clinical oncological applications of the combined PET/CT scanner include diagnosing and staging primary tumours, as well as localization of metastatic disease in almost any region of the body [BTB*00]. Further applications include decision making with respect to surgical operability of the tumour or treatment selection. PET/CT is additionally used to determine if cancer has recurred or to determine the difference between scar tissue and active cancer tissue. Especially when monitoring therapy, PET can detect changes in tumours earlier than CT, because metabolic changes occur sooner than anatomical size changes.

For a more elaborate description of PET/CT acquisition, we refer to Townsend *et al.* [TCYH04].

SPECT/CT: The benefits of combining PET and CT also extend to combining SPECT and CT. As with PET/CT, CT can provide structural anatomical information for localization, while SPECT can provide metabolic information. Similarly, CT can be used to perform attenuation correction for SPECT. SPECT is less expensive than PET, but suffers from lower contrast and spatial resolution [HH12]. A general description of the technical developments and future directions of SPECT/CT can be found in the review by Buck *et al.* [BNZ*08]. A more elaborate discussion on the clinical uses of SPECT/CT can be found in Mariani *et al.* [MBK*10].

In essence, hybrid scanners provide complimentary information that needs to be integrated, and thus fused visualizations are desirable.

3. Clinical Workflow and Requirements

In this section, we examine the clinical workflow for the analysis of multi-modal medical imaging data. Furthermore, we provide an overview of visualization requirements that should be considered when developing a novel visualization technique for such data.

3.1. Clinical workflow

Multi-modal medical imaging acquisitions are interpreted by radiologists and/or nuclear medicine physicians [ZMA08]. Since each of the two disciplines have their own specific skill set, ideally, two imaging specialists (one from each discipline) would interpret multimodal images together. However, due to availability and workload, this is often not possible [BOB*07]. Fortunately, more and more physicians are specialized in both radiology and nuclear medicine and work in joint departments. While specific protocols may vary per hospital, in general, the images are analysed similarly in radiology workstations of major vendors. The modalities can be separately analysed in the views that are common for the individual modalities, such as slice-based viewing in the axial, coronal and sagittal direction. For nuclear imaging modalities, maximum intensity projections (MIPs) are commonplace in clinical practice. Often, these MIP renderings are viewed from the front or the side of the patient. Depending on the clinical indication, more elaborate visualizations can be used, such as polar maps for cardiac SPECT data [LHG*06].

To visualize two modalities simultaneously, the typical approach in, for instance, PET/CT data is to examine the CT images in greyscale with the PET images superimposed using a colourmap in a 2D fused view (Figure 1). The combination of a coloured overlay of functional information with grey-valued anatomical information is quite effective since brightness and colour are different perceptual channels, and thus can be processed simultaneously [TG80]. Interestingly, the choice of colours in the functional colour map is not standardized and varies per vendor. For instance, while most systems map the highest activity region to red, General Electric (GE) workstations map it to blue. Common clinically used visualization combinations of PET/CT data can be seen in the work by Griffeth [Gri05]. The cases presented here are often shown with a frontal MIP of the PET, axial slices of both the PET and CT separately, and finally a fused superimposed slice of the PET and CT combined. The exact configuration of the available views may vary, but typically, there will be a central view with supporting linked views or a display featuring linked equally sized views of the different modalities and slice directions.

For oncological diagnosis and treatment planning, also the combination of CT and MRI data may be important [BHWB07]. Since these data are both high-resolution data, their combination is more

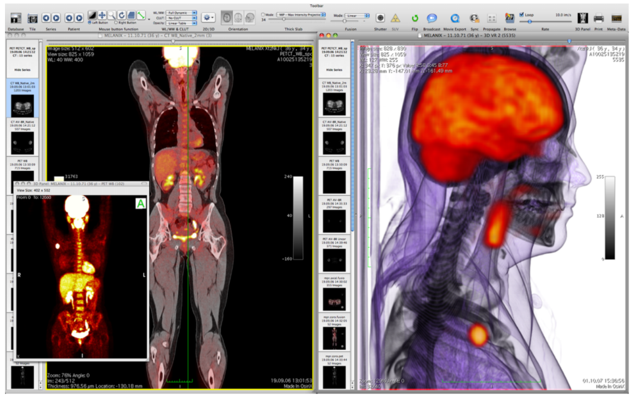


Figure 4: *2D- and 3D-fused PET/CT images with superimposed CT and PET data rendered in the OsiriX software [RSR04].*

challenging. The simultaneous exploration of CT and MRI, with either PET or SPECT, is currently not feasible with clinically available software.

While more advanced visualization techniques could be employed to visualize multi-modal images, these are not yet broadly available in clinical practice. Examples of these techniques can be found in the OsiriX software, which was specifically designed for navigation and visualization of multi-modal and multidimensional data [RSPR06]. Visualization options include multiplanar reformation (MPR), surface rendering and DVR for fused multimodal datasets (see Figure 4).

3.2. Requirement analysis

As opposed to general multi-field data, multi-modal data in medicine are acquired from a (living) patient, and scanning results may be influenced by muscle relaxation, breathing, heartbeat and movement. These local differences present special registration challenges in case of multiple acquisition techniques, and perfect matches are not guaranteed. Even in case of integrated scanners, which should reduce this problem, a perfect match cannot be achieved. The exploration of the original 2D data with the registered data superimposed may help to assess this error. Thus, 2D information are very important. When visualizing multi-field data based on simulation results, e.g. climate or technical simulations and different parameters, e.g. pressure, temperature and gradient of pressure, which result from the simulation, this registration problem does not occur, because the simulation was performed over the same domain (simulation grid). A further difference is that medical image data result from a regular grid, whereas simulation data are mostly based on irregular grids, e.g. tetrahedron, prism or hybrid grids. Thus, the resolution is often constant for medical data. For simulation data, on the other hand, coarser and finer grids may occur.

From a medical visualization perspective, the goals of multimodal medical data visualization include:

- reducing complexity and thus cognitive load,
- enabling, improving or accelerating decision making and

- providing tailored visualizations for specific applications.

In diagnosis, for instance, examining all 2D slices individually to examine anatomy, pathology and metabolic uptake can become time-consuming and cumbersome. Therefore, besides the traditional 2D approaches, 3D techniques can additionally be used to give an overview of the full datasets at a glance. Existing methods such as MIP, which was first developed for use in Nuclear Medicine [WMLK89], can provide such an overview, but suffer from depth perception issues.

3D visualization techniques that are suitable for displaying hybrid multi-modal data would allow the users to get a quick overview of areas of interest and localize, for instance, foci of elevated metabolic activity in an anatomical context. When developing a novel visualization technique or application designed for use with multi-modal medical data, there are some general requirements:

1. Visualization parameters should be easily adjustable to fit the needs of the user.
2. In order to be suitable for clinical use, the technique should be fast and interactive, with minimal or no pre-processing required.

When combining functional with structural information for diagnostic purposes, the following additional requirements should be fulfilled [LSPV15]:

1. The technique should show the combination of the two or more modalities in a fused view in which the functional activity of interest is always visible.
2. The technique should relate metabolic activity to nearby anatomical structures for accurate localization.

Such a technique can be used to guide the exploration of the datasets by bringing attention to regions of interest, after which detailed inspection of these regions can be performed in 2D images. Furthermore, besides aiding diagnosis, 3D visualization techniques could be beneficial for research and treatment planning.

For research purposes, the general visualization requirements are similar to the requirements for a diagnostic application. There are differences in the requirements in terms of the time available for users to spend on clinical versus research visualization applications. In a research setting, more time can be allocated for pre-processing and interactive analysis, while in a clinical context, there is far less time available for such tasks. Further specific requirements are application-dependent and should be formulated based on the needs of the domain experts. Surgical treatment planning could benefit from multi-modal 3D patient-specific visualization to support access planning. In oncologic neurosurgery, for instance, an access path to the tumour needs to be planned, taking the location of risk structures such as arteries into account. In this neurosurgical context, a visualization application should [BHWB07]:

- Provide high-quality, interactive and flexible 3D visualization.
- Offer multi-modal visualization for modalities such as CT, MRI, fMRI, PET or DSA.
- Provide interactive manipulation such as simulated surgical procedures, endoscopic views or virtual cutting planes.

In radiotherapy treatment planning, the pathology, i.e. radiation target, should be visualized in the context of the healthy structures at risk to receive undesired radiation damage. The requirements for such an application include [SFNB14]:

- support for 4D PET and CT data and fusion of these modalities in a 3D view,
- visualization of segmentation data,
- visualization of dose information,
- clipping and/or masking parts of the volume and
- no pre-processing and interactive parameter adjustment.

These requirements demand advanced visualization techniques to fulfil the presented requirements. In the next section, we present several visualization concepts that can be applied in multi-modal medical applications.

4. Visualization Techniques

Due to the nature of multi-modal medical data visualization, there are always two or more volumes that need to be visualized. With overlapping extents, each of these volumes may be occluded by the others, and thus no clear view can be given on the features of each of the modalities simultaneously. Visualization techniques to reduce this problem need to incorporate heuristics for *assessing the importance* of information as well as *emphasis techniques* to adjust the visualization to the derived importance. Therefore, smart visibility, focus-and-context techniques and other emphasis techniques are crucial when dealing with multi-modal medical data. In this section, we describe basic visualization techniques to cope with challenges such as dealing with occlusion, improving depth perception and presenting relevant information from multiple sources in an insightful way.

4.1. Basic techniques

For multi-modal visualization, pre-processing is often required in terms of registration or segmentation. When combining datasets from multiple modalities using separate scanners, registration needs to be performed to align the volumes. For example, Wein *et al.* proposed a fully automatic registration method to align 3D ultrasound with CT scans [WKC*07, W*07]. Segmentation is not performed routinely in all clinical applications, but, for instance, in radiation treatment planning, the target structure (tumour) and all organs at risk are segmented manually. Here, segmentation may be performed as a basis quantification for further analysis, e.g. volume measurements and selective visualizations.

Both DVR and indirect volume rendering (IVR) techniques can be applied to visualize multi-modal medical imaging data. In IVR, the marching cubes algorithm or similar is applied to a segmented subset of the image data to determine the triangulated surface mesh [LC87]. Using the resulting mesh, various shading techniques as well as different visualization methods can be applied. On such surface meshes, it is easier to perform illustrative visualization techniques such as hatching than it would be in DVR, and these techniques have the potential to be applied in multi-modal medical visualization. To determine the surface, a segmentation of the medical image data needs to be performed to select and delineate structures of interest. Since discussing alternative methods for image segmentation is out of the scope of this paper, we refer to the books by Bankman *et al.* [Ban08] and Setarehdan *et al.* [SS12] for additional information on this topic.

In contrast to IVR, DVR does not require segmentation preprocessing. In this way, there is no need to pre-determine suitable thresholds and no risk of losing critical aspects of the original data based on these choices. However, suitable transfer functions still need to be defined.

4.2. Smart visibility

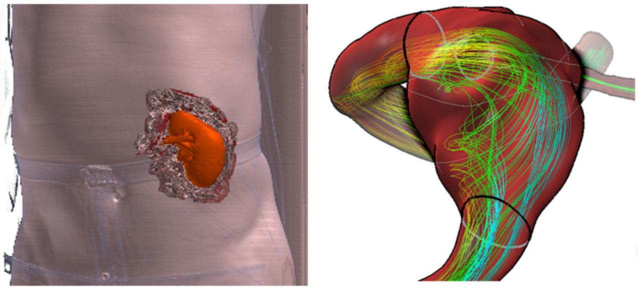
Displaying multiple structures from different modalities leads to challenging problems. Mostly, the user is interested in one specific structure, e.g. a tumour, or a class consisting of several important structures. These important structures may be surrounded by other objects, resulting in structures that may occlude or overlap each other. In the following, we describe advanced visualization techniques that require the important structures to be segmented.

A primary concern is how to resolve the occlusion problem such that the most important structures are clearly visible, while still indicating surrounding structures. Hiding the surrounding structures is not appropriate, since they provide spatial context. Whenever interesting objects are occluded, smart visibility techniques can be applied. For the smart visibility term, we refer to Viola and Gröller [VG05] who gave the following definition: 'Expressive visualization techniques that smartly uncover the most important information in order to maximize the visual information in the resulting images'. This visualization technique category comprises several sub-categories and different ways to remedy the occlusion problem. Here, we introduce the most prominent ways to resolve visibility problems consisting of cutaways and ghosted views, and present preliminary guidelines on how they could be applied to multi-modal medical data.

4.2.1. *Cutaway views*

Cutaway views provide a way to depict a focus object and to separate it from the surrounding context structures. Cutaway views employ, for instance, a conic object placed around the focus object. The conic object is aligned towards the camera in such a way that the camera looks inside the object from the base to the tip. Every non-focus structure that is inside the conic object is cut such that only the focus object inside the cone is visualized. The main advantage is the clear illustration of the main object without occlusion by the surrounding objects. Unfortunately, structures between the focus object and the view point of the camera are lost. In general, cutaways vary from *pre-defined models* [LHV12] to *focus-oriented objects* [BF08, KTP10].

Pre-defined models: With pre-defined models, view-dependent and view-independent approaches can be distinguished. Independently, the pre-defined model is loaded into the framework and subsequently all structures are tested to see if they are inside or outside the focus object. For instance, a lymph node can be approximated by a cylinder with a suitable size. Here, during the rendering, an inside/outside test can be applied to the surrounding (context) objects with the pre-defined model. In case the context objects overlap with the pre-defined model, the fragments are discarded; otherwise, the fragments are drawn. Mostly, view-dependent cutaway techniques are used, where the conic objects are oriented along the view-vector. Pre-defined models can be used if the focus object has a simple shape. Moreover, it is also only applicable if the model does not vary over time. In case of animated blood flow, pre-defined models cannot be employed, due to the change of the form and position of the blood flow [LGV*15].



(a) (b)

Figure 5: *Examples of smart visibility techniques applied to medical data: a cutaway revealing the kidney inside the abdomen based on CT data [VKG04], and blood flow showed inside an artery using a ghosted view based on a mesh and simulation data [GNKP10].*

Focus-oriented models: The second class of cutaway techniques uses focus-oriented models. Here, the conic object is constructed based on the focus object and can be arbitrarily shaped. To achieve real time performance, the determination of the conic object and the associated cutaway needs to be efficient. Previous work, such as the work by Viola *et al.* [VKG04], uses a Chamfer distance transform approximation [Bor86] to the conic object in order to calculate the cutaway (see Figure 5 a). Thus, a depth image of the conic surface is calculated, which is then used to cut away regions that are closer to the viewer than the conic object itself. Other approaches were developed to speed up this calculation [RT06]. Here, the cutaway surface function C is defined by:

$$C(p) = \max_{q \in R}(q_z - m \cdot \|q_{xy} - p_{xy}\|),$$

where R contains the focus object, m defines the slope of the cone by $m = \tan^{-1}\theta$ and p_{xy} is the pixel's current 2D location. The key idea is to determine the conic object in the view plane with a jump flooding algorithm. Usually, the conic object is generated by applying the standard flood fill, an iterative process in which in every iteration, a pixel passes its value to its direct neighbours. Contrarily, the jump flood algorithm uses the same approach, but the neighbours vary for each iteration. Thus, a pixel passes its value to its neighbours, which have a certain distance, and for each iteration, the step size is halved. Cutaway generation was used to visualize animated blood flow in such a way that a clear view on the blood flow within a vessel is always guaranteed [LGP14].

Application to multi-modal data: Cutaway views can be directly employed in multi-modal visualization. For instance, one modality could be displayed outside the cutaway region, while another is displayed within the cutaway. Furthermore, cutaways can be used on both modalities to reveal structures of interest hidden within a larger anatomical structure.

For instance, a cutaway can be used to display hybrid imaging PET/CT data, where high PET activity needs to be depicted. By using a cutaway view in these regions, the high PET activity is always visible and it provides a clear view inside the anatomical CT data and can provide a correct localization of the occurrence, whereas a simple MIP cannot give reasonable depth cues. Such a view might be useful not only for diagnosis, but also for patient–doctor and interdisciplinary communication, as well as for treatment planning.

4.2.2. *Ghosted views*

An easy way to illustrate the focus object and the surrounding objects is to use transparency. The main drawback of employing multiple transparent objects is that they may lead to visual clutter. Furthermore, it is hard to interpret the shape and ordering of overlapping regions. To remedy this, ghosted view techniques attempt to improve the transparency depending on the underlying object. Here, a distinction can be made between smart transparency techniques and interactive approaches. In smart transparency, the strength of transparency depends mostly on curvature or normal vector information. One approach is to set the transparency very high if the surface is nearly planar and to increase the opacity if the curvature varies. That helps to identify regions where the morphology changes strongly. This was successfully applied, for instance, to vessel visualization with embedded flow [GNKP10, GLH*14], an example of which can be seen in Figure 5(b). The transparency is set by $F = 1 - \langle V, N \rangle^r$, where V represents the view vector, N the surface normal and r represents the shininess constant. The superiority of this approach over standard semi-transparent visualization related to cerebral blood flow was confirmed in a perceptual study by Baer *et al.* [BGCP11].

An additional transparency technique was inspired by suggestive contour lines, a line drawing technique that emphasizes characteristics of the surface. This approach was used to develop a shading approach, based on a suggestive contour scalar field [LGP14]. Here, the scalar field is used to determine zero-crossings after which positive and negative values are used to shade the object in orange or cyan, respectively.

Application to multi-modal data: Ghosted views can be applied to multi-modal data visualization in order to remove emphasis of structures that are less important from one or more modalities. A ghosted view can be employed to show an anatomical context in order to localize functional data without occluding the view. For instance, a brain surface can be rendered as a ghosted view, while functional data are rendered in an opaque style. This yields a visualization where the brain surface can be recognized, without being occluded, whereas the functional brain data are directly depicted. The main challenge is to provide a transparency technique that is not disturbing, but provides as much morphological context as possible, while not occluding underlying structures. Conventionally, a simple transparency setting is used, which does not provide much shape information.

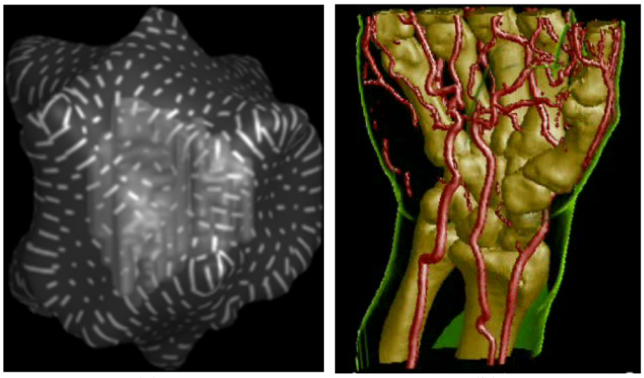


Figure 6: *One of the first focus-and-context illustrations with hatching patterns used for the isosurface of radiation dose along with a tumour to be destroyed (©[1996] IEEE. Reprinted, with permission, from [IFP96]). On the right, a focus-and-context visualization applied to a hand data set with arteries [HMIBG01].*

4.3. Focus-and-context visualization

For focus-and-context visualizations, we assume that at least the focus object is segmented. Even though a lot of techniques exist that provide insight into the focus object, the question is how to represent them in the context of the surrounding structures. A straightforward approach is to use the same shading technique on all structures, which may lead to a hindered perception of the focus object by the context objects. Thus, the main goal of the *focus-and-context* visualization is to illustrate the focus object so that it is perceivable, and simultaneously illustrating the surrounding context structures without distracting from the focus. Techniques vary from using unsaturated colours for shading, to different shading methods per object class, to even varying entire rendering concepts.

Line drawings. One of the first line drawings that appeared in combination with focus objects was presented by Interrante *et al.* [IFP96]. They used a hatching technique for the surrounding objects which are represented by the isosurface of radiation. In this case, anatomical data are combined with a scalar field resulting from the simulation of dose distribution, performed for radiation treatment planning. The lines were aligned along the principle curvatures directions for an improved shape perception, whereas the inside focus object was simply shaded (see Figure 6a). Another line drawing technique that appeared in combination with focus objects was presented by Treavett and Chen [TC00]. They developed line drawings that can be applied on volume data sets and furthermore showed how they can be used to illustrate the surrounding context object, e.g. the skin, with the focus object, e.g. the skull. Again, in the context of volume rendering, Hauser *et al.* [HMIBG01] used combined visualization techniques to illustrate different objects. For instance, bones are rendered with DVR, surface rendering is applied to the vessels and contours indicate the skin (see Figure 6b). Lum and Ma [LM02] presented a way to render a dataset with non-photo-realistic techniques efficiently. Several illustrative techniques can be applied with interactive frame rates. It was shown that line drawing concepts can successfully be used for focus-and-context

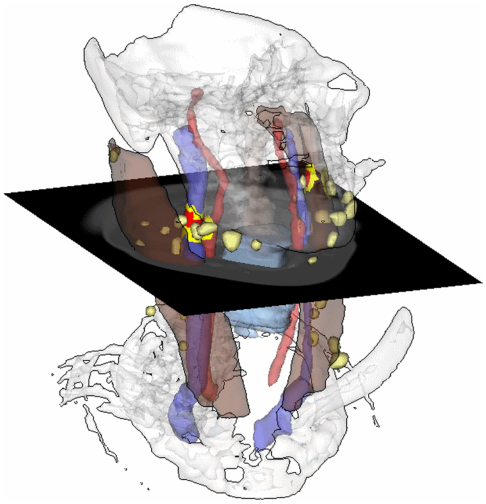
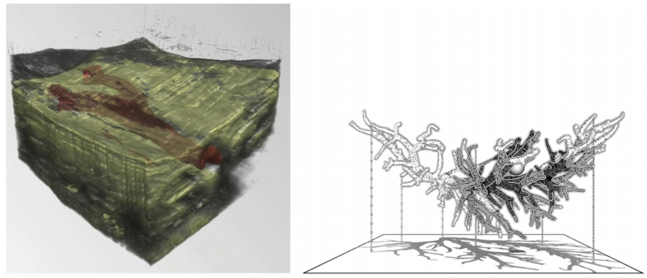


Figure 7: *A focus-and-context visualization applied to a CT scan of the neck revealing lymph nodes and vascular structures with a slice of imaging data [TMS*06].*

visualization [TIP05]. The core idea here was to provide the flexibility to combine surface, volume data and line drawing for a sparse visual representation of context objects. Here, not only line drawings, but illustrative visualization techniques, in general, were used to visualize context objects. The key idea of illustrative visualization is to provide a simplified and expressive depiction of a scene or problem [Law15]. Here, details are omitted purposefully in order to convey only the important information.

Tietjen *et al.* combined and tested [TIP05] various rendering techniques. While their technique was not shown on multi-modal data, it is applicable for feature fusion. Later, Tietjen *et al.* [TMS*06] used slice-based visualizations in combination with 3D illustration techniques (see Figure 7) for an example of focus-and-context visualization in the medical context. In a similar way, a slice or slab of CT/MRI data may be integrated in an SPECT/PET visualization or vice versa. The slice/slab may be even enhanced with contours from a segmented object. For PET/CT, Kim *et al.* [KEF07] used different rendering techniques to illustrate the PET enrichment and the anatomical context by using the CT data. Various rendering techniques were also used in the context of simultaneously rendering anatomical and functional brain data [JBB*08]. For an overview of focus-and-context approaches, we refer to Cohen [Coh06] and Bruckner *et al.* [BGM*10]. Another importance-based DVR approach was presented by Pinto and Freitas [dMPF10, dMPDSF11]. Furthermore, they combined standard volume rendering approaches with illustrative visualization techniques (see Figure 9). For focus-and-context visualization with PET/CT hybrid data, Bramon *et al.* [BRB*13] suggested visualization techniques to emphasize the PET activity. Another approach to explore and visualize interesting regions was proposed by Abellán *et al.* [ATGP13]. They demonstrated their approach on MR/PET data, and used illustrative visualization techniques to convey information.

Lens-based visualization. Focus-and-context visualization can also be applied interactively, e.g. with *magic lenses* that can be used to look through objects and to reveal interesting parts [BSP*93]. The magic lens can be applied in many situations, ranging from whole body that uses a lens to reveal organs, to vessels where a lens depicts special properties of the blood flow [GNBP11]. A special application in medicine is to employ the vertical symmetry of the human body and propagate the movement of the lens in one part of the body to the other part, thus supporting the comparison between a suspicious region and the analogue region on the other part of the human body. For 3D ultrasound, Schulte zu Berge *et al.* [SzBBKN14] presented a framework where the user can set various predicates such that interesting regions are highlighted. Increasing the slider for the vessels makes it more visible than the surrounding structures (see Figure 8a). In the context of vascular models and tumour visualization, Lawonn *et al.* [LLPH15] presented a way to depict the vessels with line drawings techniques, while the tumour is visualized with diffuse shading (see Figure 8b). Furthermore, lenses can also be employed to control which source is displayed, e.g. in the lens region PET (or PET and CT combined) and outside only CT. Thus, different layers may be shown interactively [KSW06].



(a) (b)

Figure 8: *Focus-and-context visualization of a 3D ultrasound dataset where the arteries are shown [SzBBKN14] and a visualization where vessels and a tumour, reconstructed from CT data, are illustrated with line drawings [LLPH15].*

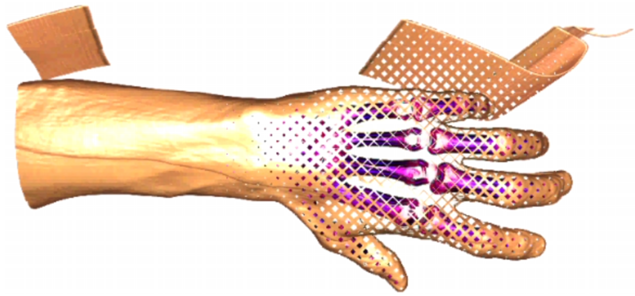


Figure 9: *Focus-and-context visualization based on a CT scan of the hand and wrist. The bones are shown by applying a cutaway technique [dMPF10, dMPDSF11].*

The distinction between smart visibility and focus-and-context visualization is not that clear. We argued that focus-and-context visualization techniques are a sub-category within the broader category of smart visibility approaches. The main goal of smart visibility is to provide insights into interesting regions or objects, but this goal can also be achieved by adding 2D image planes in a 3D visualization representation [HE98, BHW*07]. In this case, there is no focus object involved, although it is still clearly a smart visibility technique. Thus, we consider focus and context visualization a subgroup of smart visibility techniques, which is a broader category including cutaways, ghosted views or exploded views, as well as techniques in which there is no focus object.

Application to multi-modal data: Focus-and-context techniques are applicable to multi-modal medical data and can be employed in two main ways. First, both modalities may be combined and a region of interest within the datasets can serve as a focus area, while the context is rendered in a different style. Secondly, one modality with a higher importance can be rendered as the focus dataset, while the other is rendered to provide context. The rendering style required strongly depends on the application. For instance, if the focus region consists of a tumour and the physician is interested in the distance to nearby vessels for anatomical context, then the complete morphological vessel structure may be not as important as an indicated position of the nearby vessel structures. In this case, a simple contour that shows only the outline and allows for fast recognition of the spatial extent may be sufficient. But in case of a liver tumour, the spatial impression and the shape of the liver is important for treatment planning. In this case, a more advanced approach needs to be applied to illustrate the tumour in a reasonable way, while simultaneously depicting the liver surface with important spatial and morphological features. Different rendering styles may be used for multi-modal visualization, e.g. contours representing boundaries of objects in one modality may be overlaid to the visualization of a second dataset, where no contours are used.

4.4. Summary

There are different channels with which we perceive information, e.g. colour, or orientation of elongated objects. Thus, we can perceive information simultaneously if it is encoded in different channels. The major theory here is the Feature Integration Theory, developed by Anne Treisman [TG80]. Multi-modal visualization applications may benefit from the use of different visualization techniques that can be easily perceived simultaneously, e.g. colour is only used for depicting one dataset, and line drawing techniques for the other. In order to represent multiple modalities in a single rendering, smart visibility techniques are crucial to prevent visual clutter and occlusion problems. Specifically, multi-modal medical visualization can benefit from deciding which dataset has priority, i.e. the 'focus dataset', and which is the context dataset. In multi-modal visualization design, one could consider indicators of importance of a modality, such as the size and resolution, which could, for instance, be indicative of which dataset is best used for anatomical detail. Then, one could think about which techniques are primarily suitable to show the focus dataset, likely revealing more details, and which to show the context dataset. This approach forms a bridge between single data focus-and-context techniques and focus-and-context in the context of multimodal data. There may also be situations where both volumes have the same importance, e.g. CT and MRI, and in these situations, it might be more appropriate to consider a region within both datasets the focus area, while the region outside is rendered as context. In conclusion, visualization techniques that have

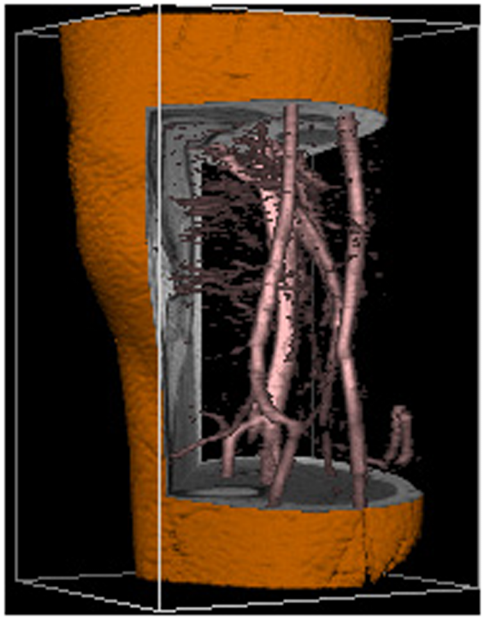


Figure 10: *First multi-modal volume rendering technique by Höhne* et al. *visualizing vascular MRA and anatomical MRI data simultaneously [HBTR88].*

been developed for single modality visualization can be adapted to multi-modal data, but this requires careful consideration of the application area requirements and in some cases extensions of existing techniques.

5. Rendering and Interaction Techniques for Multi-Modal Data Visualization

In this section, we discuss rendering and interaction techniques for multiple or fused volumes. First, we discuss recent contributions on rendering aimed at fusing multiple volumes together at different points in the rendering pipeline. After this, we discuss interaction techniques that are designed for use with multi-modal medical data, including clipping and specialized transfer functions.

5.1. Rendering techniques

In this subsection, we provide an overview of rendering techniques suitable for rendering two or more volumes simultaneously. Although Drebin [DCH88] and Levoy [Lev88] are often cited as the developers of the first volume rendering approach, actually Höhne [HB86] was the first to render a volume based on CT data. As a follow-up, Höhne [HBTR88] was also the first to develop a multi-modal visualization technique visualizing MRI combined with MRA (see Figure 10). Cai and Sakas presented a seminal work that allows rendering of multiple volumes [CS99]. They presented a method to achieve a reasonable mix of opacity, colour and illumination. Furthermore, they defined three levels of volume intermixing:

- illumination model-level intermixing,
- accumulation-level intermixing and
- image-level intermixing.

In illumination model-level intermixing, the opacity and intensity at each sample point are calculated directly from a multi-volume illumination model, instead of mixing several opacity and intensity values. This type of volume intermixing is the most complex, but also the most realistic. In accumulation-level intermixing, the intermixing is performed during ray sample accumulation by mixing opacities and intensities from different volumes. This method requires changes to the rendering pipeline and the time consumption can be high, but provides correct depth cues. The simplest intermixing method is image-level intermixing, where the two rendering images are merged on the pixel level. For this, no changes need to be made to the rendering pipeline, but there is a lack of correct depth cueing. This approach was successfully applied in the context of radiotherapy treatment planning, combining CT, dose and segmented object volumes.

Wilson *et al.* presented a visualization approach to depict different image modalities together at interactive frame rates using different rendering styles [WLM02]. To render the result efficiently, they used the GPU and demonstrated their results with two case studies. One of the case studies featured a multi-modal mouse data set combining PET and MRI acquisitions. Ferre *et al.* discussed strategies to visualize multi-modal volume datasets using direct multi-modal volume rendering (DMVR), in which they determine in which steps of the rendering pipeline data fusion must be performed in order to accomplish the desired visual integration [FPT04]. Furthermore, they stated requirements and proposed five rendering methods that differ in the step of the rendering pipeline at which the fusion is performed: property, property and gradient, material, shading and colour fusion. They used SPECT and MRI data to present a combined visualization and evaluate the suitability of the five methods for this data. Another technique to render multi-modal volumes, which additionally solves depth cueing issues with reduced time consumption, was presented by Hong *et al.* [HBKS05]. They conducted experiments that showed that their method can distinguish the depth of overlapping regions and produces rendering results faster than conventional software using High Level Shader Language (HSLS) for efficient volume fusion. They show the results of their method on PET and CT images in a performance evaluation. Rößler *et al.* described a GPU-based multi-volume rendering scheme that allows users to visualize an arbitrary number of volumes interactively, focused on fMRI data [RTF*06]. Subsequently, they introduced dynamic shader generation for multi-volume ray casting, by allowing users to define an abstract render graph, to overcome the fact that typically shaders can only be programmed by GPU experts [RBE08]. In an accumulation-level volume rendering context, their system automatically generates different shaders per volume from the configuration of an interactive abstract render graph. Brecheisen *et al.* employed a framework to render different volumetric datasets together [BBPtHR08]. They used depth peeling to visualize overlapping volumes that can be intersected with an arbitrary number of geometric shapes. Kainz *et al.* proposed a framework for rendering multiple volumes on the GPU [KGB*09]. Theirs was the first framework for multi-volume rendering that still provided interactive frame rates while rendering over 50 arbitrarily overlapping volumes. Recently, Sunden *et al.* introduced a volume illumination technique specifically designed for use with multi-modal data [SKR15]. They proposed a new *light-space-based* volume rendering algorithm, which employs illumination-importance metrics to compress and transform multi-modal data into an illumination-aware representation. Their method was applied to CT and MRI data, as well as microscopy and simulation data and evaluated based on the quality and performance. Lindholm *et al.* [LFS*15] presented a rendering algorithm for hybrid volume-geometry data. They combined volume data and geometry-based data, i.e. a mesh. They applied their approach to proteins, vessels with blood flow and DTI. Additional related work can be found in the state-of-the-art report on the visualization of multivariate scientific data presented by Fuchs and Hauser [FH09]. Schubert and Scholl provide a performance and perceptual comparison of GPU-based multi-volume ray casting techniques [SS11]. Furthermore, they presented an overview of visualization techniques that use data intermixing approaches and DVR methods that use ray casting. They add classification-level intermixing to the three levels defined by Cai and Sakas [CS99], which mixes volumes by linear combination of the sample values at the beginning of the rendering pipeline. For a general overview of large-scale volume visualization techniques, we refer to the state-of-the-art report by Beyer *et al.* [BHP15].

In the area of medical image fusion, Gupta *et al.* [GRB08] presented a measure to evaluate PET/MRI image fusion. They confirmed the usefulness of their approaches in different experiments. For this, they used an entropy measure to combine the interesting parts in PET and MRI, but this approach was also applied to CT combined with MRI. Lindholm *et al.* introduced fused multi-volume DVR using a binary space partitioning (BSP), aimed at medical volume rendering of multi-modal data [LLHY09]. Lindholm *et al.* provided a GPU-based ray-casting approach to visualize intersecting volumes with regard to an efficient depth sorting of the resulting fragments. Bramon *et al.* fused image modalities and applied their technique to CT, MRI and PET data [BBB*12]. This information-theoretic framework automatically selects the most informative voxels from two volume datasets. They evaluated the potential of their technique with medical experts and concluded that it is potentially useful for planning radiotherapy, treatment monitoring and planning brain surgery. In their evaluation, they proposed several information maps and fused data sets and had the experts vote on the quality. Their method performed well in differentiating between bone and cerebral tissue, as well as between morphological and functional data. More recently, Kim *et al.* introduced a slab-based intermixing method for fusion rendering of multiple medical objects [KKL*16]. We refer to James and Dasarathy [JD14] and Galande and Patil [GP13] for a more extensive discussion.

5.2. Interaction techniques

In this subsection, we describe several interaction techniques that were successfully used in the context of multi-modal medical data. Interaction techniques primarily serve to adjust which portions of the dataset are visible. Visibility may be adjusted with clipping and cutting on a geometrical basis and with transfer functions on the basis of attribute values, e.g. intensity values, gradient magnitude or curvature.

Clipping and cutting. In the work by Hastreiter *et al.*, clipping planes were employed per volume to cut separate modalities in different ways [HE98]. This can be used to look at the slices while simultaneously analysing the 3D visualization. Furthermore, they

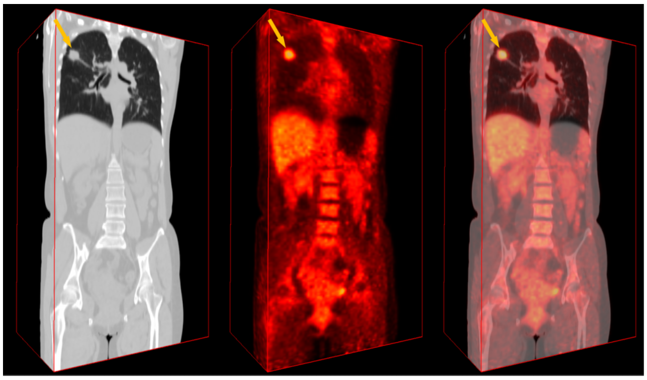


Figure 11: *PET/CT data are mixed to visualize the volume in a single view [KEF07].*

combined CT and MR images in a single view. Fairfield *et al.* proposed a custom clipping solution for co-registered MRI and CT, which they refer to as 'curtaining' [FPJ*14]. This allows the user to define a clipping region in which the other modality will be shown. Manssour *et al.* propose a method to visualize inner structures in multi-modal volume data employing cutting and data intermixing [MFO*02]. They applied it to the skull where cutting planes were used to analyse the brain. More advanced ways of clipping data were developed by Weiskopf *et al.* via per-fragment operations in texture-based volume visualization [WEE02]. While their method was applied to a single modality, their technique was successfully employed by Rößler *et al.* to clip the brain based on regions in an atlas of the human brain combined with fMRI data [RTF*06]. More recently, a membrane clipping approach was proposed that avoids cutting through features in the data [BBBV12]. While it was not directly applied to multi-modal datasets, it could be used in such a way. Furthermore, their technique features slab rendering which is a trade-off between slice-based viewing and full 3D rendering.

Transfer functions. To tackle occlusion problems, transfer functions are essential and have been designed for multi-modal data. 2D transfer functions, introduced by Levoy in 1988 [Lev88], are an essential method for multi-modal visualization, since they allow the user to emphasize boundaries and details within structures. Kniss *et al.* applied a multi-dimensional transfer function to multivariate weather data that allow experts to readily identify specific zones for their analysis task [KHGR02]. They presented a case study in which they explore the utility of multidimensional transfer functions for the visualization of multivariate fields. Furthermore, Dobrev *et al.* proposed to a hierarchical clustering approach for visual analysis of multivariate volume data, which allows the user to operate in cluster space, rather than transfer function space [DVLL*11]. Kim *et al.* introduced a dual-lookup table for PET/CT data such that medical experts can set different transfer functions for every volume in a single view [KEF07]. They provided techniques such that the volumes can be merged properly with different transfer functions, see Figure 11. A general information-based approach for transfer functions was introduced by Haidacher *et al.* [HBKG08]. They provided a transfer function space to visualize certain tissues of multi-modal data. They applied their method successfully to PET/CT data of the brain.

Joshi *et al.* introduced new interaction techniques to explore and visualize multi-modal data [JSV*08]. Their technique allows for a precise control of the shape of the region in the brain that can be used to crop data during exploration and surgery. For their approach, they used SPECT/MRI and fMRI data. Additionally, Ropinski *et al.* proposed interaction techniques to show a close-up of an interesting region in the context of the rest of the data [RVB*09]. They applied their technique to PET/CT data registered with MRI. More recently, Haidacher *et al.* proposed an approach for volume analysis based on multi-modal surface similarity [HBG11]. With this, the similarity space generated can be used for isosurface selection in applications like dual-energy computed tomography (DECT). The similarity map can be used to set different isovalues, e.g. for DECT, such that inner structures can be set opaque, whereas outer structures can be set as transparent. Correa and Ma [CM11] employed visibility-driven transfer functions to illustrate important structures in comparisons to the surrounded regions. Their approach provides the user with graphical cues that inform about the contribution of particular scalar values to the final image. Furthermore, they presented a semi-automatic transfer function design that solves an energy minimization problem, such that the visibility of an initial opacity transfer function that provides the desired importance is maximized. A complete survey on transfer functions for volumetric data can be found in the work by Ljung *et al.* [LKG*16].

6. Applications

In this section, we provide an overview of recent multi-modal medical visualization papers that are application-oriented. We further subdivide this section in applications developed in a research-oriented, diagnosis or treatment planning and guidance context. For diagnostic purposes, we distinguish applications developed for cardiology and those aimed at oncology. The treatment planning and guidance applications are further categorized into neurosurgery and radiotherapy planning.

6.1. Medical research

Multi-modal medical data visualization applications were developed in a research context related to vascular pathology development as well as neuroscience. Rößler *et al.* described a GPU-based multi-volume rendering scheme that allows users to visualize an arbitrary number of volumes interactively (recall Section 5.1.1), and their technique was specifically focused on functional brain images [RTF*06]. Their tool was aimed at supporting cognitive neuroscientists in experimental studies and to communicate results to non-experts and employs a template brain with patient-specific fMRI data (see Figure 12). PET/CT scans are often requested in cases related to clinical oncology for initial cancer staging or a follow-up during or after treatment [BOB*07]. However, Ropinski *et al.* visualized mouse aorta PET/CT scans in a medical research-oriented application related to the formation of plaque [RHR*09].

They propose a linked multi-view approach, using a specialized straightened multi-path curved planar reformation combined with a multi-modal vessel flattening technique (see Figure 13). In a follow-up work, Diepenbrock *et al.* additionally looked into PET/CT visualization of mice arteries [DHS*13]. They used the vessel wall

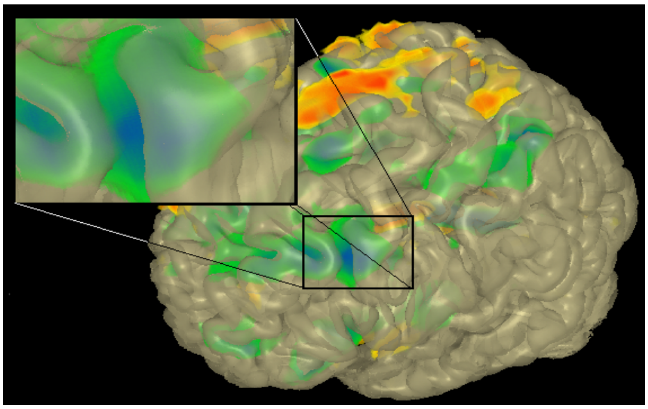


Figure 12: *A non-polygonal isosurface revealing patient-specific functional information in anatomical context of a template brain [RTF*06]. Image courtesy of the authors.*

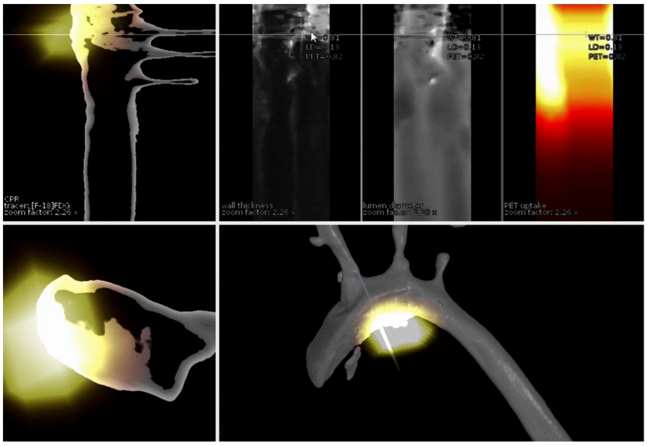


Figure 13: *Multiple linked views allow for comparative visualization of vascular PET/CT in mice [RHR*09].*

extracted from the CT scan to perform a normalized circular projection which allows the user to judge PET signal distribution in relation to the deformed vessel.

Nguyen *et al.* used an approach to visualize and interact with real-time fMRI data in a neuroscience research context [NOE*10]. They treat the fMRI signal as light emission and render it in the context of a patient-specific high-resolution reference MRI scan. Using this technique, the brain glows and emits light from active functional regions with a 2 s delay of the measured fMRI signal. In the work by van Dixhoorn *et al.*, the focus is on examining whole-brain functional network connectivity at a voxel level [vDMvLB12]. They visualize the correlation of the functional activity, where fMRI time signals at each voxel are correlated with every other voxel in the brain to determine functional connectivity. Therefore, they propose an application for the interactive visual analysis of this high-resolution brain network data, both in a linked matrix representation as well as in its anatomical context based on MRI in a GPU ray-casting framework.

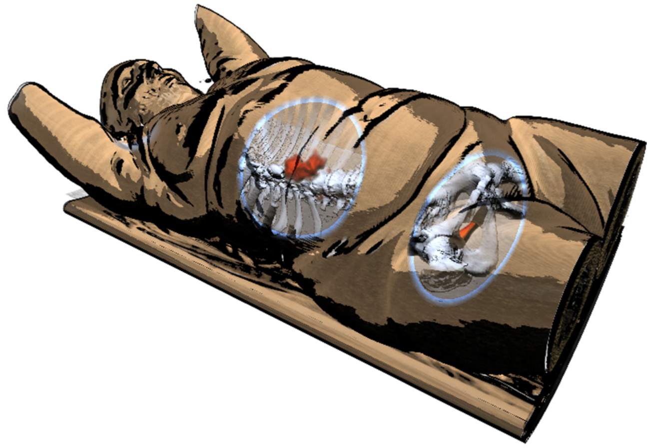


Figure 14: *PET/CT visualization with PET activity presented as a focus area using dynamic cutaways and CT providing anatomical context for accurate localization [LSPV15].*

6.2. Diagnosis

Visualization techniques aimed at improving diagnostic value of multi-modal medical data have been primarily developed in the fields of oncology and cardiology.

6.2.1. *Oncology*

Among the oncological applications, Kim *et al.* introduced a dual-lookup table specifically designed for use with PET/CT data such that medical experts can set different transfer functions for every volume in a single view [KEF07]. Jung *et al.* employed a novel visualization approach by integrating a *visibility-driven transfer function* specifically for PET/CT data [JKE*13]. Furthermore, they provided an intuitive region of interest selection tool for further exploration. Lawonn *et al.* recently developed an illustrative technique for focus-and-context rendering of PET/CT data [LSPV15]. In their approach, the functional information from the PET data is used as the focus, while the CT provides anatomical context using dynamic cutaway views (see Figure 14). Viola *et al.* presented illustrative techniques to visualize liver ultrasound combined with CT information serving as anatomical context [VNØ*08]. They aim to shorten the long learning curve for ultrasound practitioners in training, as well as assist the interpretation of liver examinations.

6.2.2. *Cardiology*

Due to the severity and frequency of cardiac diseases, this application area is of utmost importance. Essential diagnostic tasks include plaque assessment in the coronary arteries, detailed diagnosis of a heart infarction, e.g. the extent of infarct core, assessment of the heart valves and assessment of abnormalities, such as congenital heart failures. Morphological information, extracted from CT and MRI, as well as functional information, e.g. wall motion extracted from ultrasound, are important.

An example of a multi-modal visualization problem that was considered in visualization research is the use of perfusion data

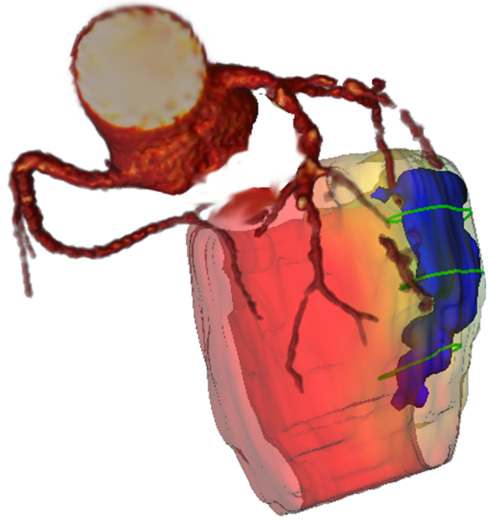


Figure 15: *Combined visualization revealing an infarcted area in dark blue, with hypo-perfused regions represented by contours. The myocardium is shown as a transparent coloured surface that encodes the distance to the infarction [HSF*08].*

combined with other MR imaging modes of for the diagnosis of the coronary heart disease. Perfusion data of the heart, which indicates the blood perfusion in the myocardium and can be acquired from MRI or SPECT scanners, need to be combined with anatomical data to provide morphology of the heart muscle and the coronary arteries. Similar to combining PET and CT data, the resolution of the perfusion data is much coarser. Moreover, the acquisition of cardiac perfusion data exhibits gaps, i.e. there are regions in the morphological data where no corresponding perfusion data are available. Simply interpolating the missing information is not a satisfactory solution. Thus, the overlay of both information must convey where slices of the morphological data correspond to morphologic slices and where no such correspondence exists. Termeer *et al.* proposed a visualization for the diagnosis of coronary artery disease using cardiac perfusion MRI data [TBB*07]. They extend the traditional bull's eye plot to a continuous volumetric version that reveals transmurality of scar tissue and links this to an anatomical view of the heart. Transmurality indicates whether the whole wall of the (left) ventricle is affected by an infarction—information that is essential for prognosis and treatment. Oeltze *et al.* presented an integrated multi-modal visualization of morphologic and cardiac perfusion data for the analysis of coronary artery disease [OKG*06]. Myocardial perfusion is measured using an MRI scanner and combined with CT coronary angiography (CTCA) which depicts the anatomy. In their visualization, coloured icons, heightfields and lenses are used to visualize and explore the different parameters measured. Hennemuth *et al.* developed a comprehensive approach to the analysis of contrast-enhanced cardiac MR images [HSF*08]. They propose a full workflow to align the different datasets, extract surfaces and analyse them in a combined way (see Figure 15). Kirişli *et al.* combine CT angiography (CTA) and SPECT myocardial perfusion imaging (MPI) in a visualization aimed at assessing coronary artery disease [KGS*14]. They evaluated the diagnostic value of a software-based image fusion system over conventional side-by-side analysis and found improved diagnostic performance when using their application.

6.3. Treatment planning

Multi-modal medical data visualization applications have been developed mainly in the areas of neurosurgical planning and guidance. Some recent works have focused on radiotherapy treatment planning.

6.3.1. *Neurosurgery*

A primary focus in neurosurgical planning applications is identifying surgically relevant structures that are at risk to be damaged, such as the functional areas in the grey matter and the white matter fibre tracts, and understanding how they are related to the lesion that needs to be removed. The surgically relevant structures can be acquired using CT, MRI, fMRI, DTI as well as different MR protocols. Additionally, neurosurgeons need to plan a safe access path to such a lesion, with the least amount of damage to vital functional areas, derived from fMRI, and fibre tracts, derived from DTI. Visualization applications aimed at neurosurgical planning and guidance often focus on brain tumour resection, but also applications aimed at deep brain stimulation (DBS) and arteriovenous malformations (AVMs) surgery exist.

Jannin *et al.* fused several modalities and imaging modes from MRI for neurosurgery navigation [JFS*00]. They combined segmented structures and vessels with functional areas from magnetoencephalography (MEG) and fMRI data in a neuro-navigation application. As one of the most notable early techniques where surfaces are used for combined information, Stokking *et al.* presented a visualization method that combines functional input data and a surface extracted from anatomical data [SZV01]. They map fMRI values onto a brain surface using the surface normal and evaluate their technique on both registered (S)PE(C)T/MRI and fMRI/MRI. This technique was an extension from earlier work on combining software-registered SPECT with a surface extracted from an MRI scan, by mapping functional values of the SPECT to the surface of the brain along the normal [SZP*97]. While these techniques were applied to the brain, the idea of using a surface can be transferred to other organs, such as the heart muscle. Blaas *et al.* proposed an approach that fuses fMRI and DTI data for planning brain tumour resections [BBM*07]. In this fused volume, users can extract fibre bundles that pass through a region around the tumour. These bundles can then be explored by filtering on distance to the tumour, or by selecting a specific functional area using arbitrary convex geometries as selection criteria (see Figure 16).

Rieder *et al.* employed a combination of fMRI and DTI data for neurosurgical planning [RRRP08]. Their application visualizes pathologies using a distance-based transfer function, as used in the work by Tappenbeck *et al.* [TPD06], and only shows functional data in close proximity to the lesion. Furthermore, they increase depth perception by including a distance-ring, which visualizes how deep the lesion is situated in the brain from the current viewpoint. For the surgical planning itself, they provide access path visualization and rely on identification of superficial landmarks which can be translated to the per-operative context (see Figure 17). A visualization

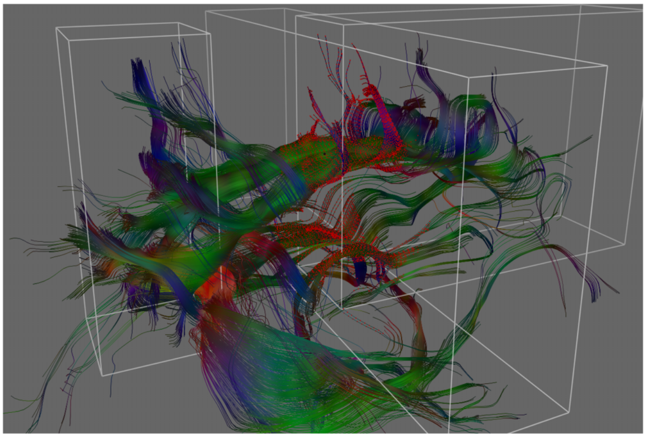


Figure 16: *Fibre bundle filtering using multiple boxes to select bundles with arbitrary logic combinations for selection of fibres to be shown in multi-modal visualization [BBM*07].*

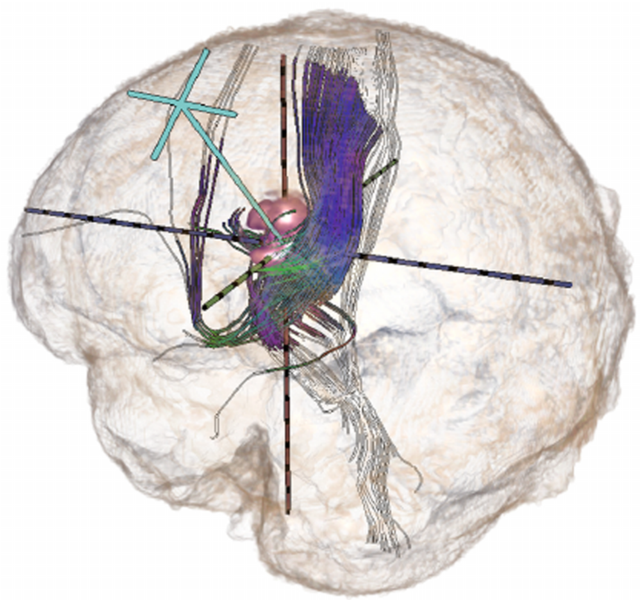


Figure 17: *Path planning application for oncologic neurosurgery based on MRI, fMRI and DTI data [RRRP08].*

approach for combined MRI and fMRI brain data was presented by Jainek *et al.* [JBB*08]. Various rendering styles were used, e.g. ambient occlusion, and illustrative techniques were employed to enhance the visual output. Following up on this work, Born *et al.* extended it to include DTI tracts, which reveal reconstructed nerve fibres that connect functional areas [BJH*09]. They also enhanced depth and shape perception by applying silhouettes and dithered half-toning (see Figure 18). Janoos *et al.* proposed a method to visually analyse brain activity from fMRI data, with a special focus on temporal dependencies [JNM*09]. They propose a methodology to analyse the time dimension through volumes-of-interest, of which the selection is guided by a hierarchical clustering algorithm in the wavelet domain. They visualize these volumes-of-interest overlaid

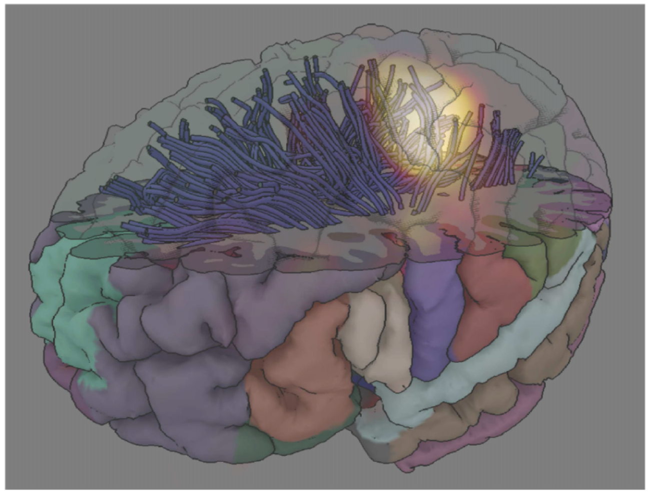


Figure 18: *Visualization of cortical anatomy (MRI), brain activity (fMRI) and nervous pathways (DTI). Springer [BJH*09], ©Springer-Verlag Berlin Heidelberg 2009. With permission of Springer.*

onto MRI data of the brain and show the cluster time series of selected clusters in a separate view.

Diepenbrock *et al.* were the winners of the IEEE VIS Visualization contest on multi-modal visualization for neurosurgical planning [DPL*11]. They provided a 3D view inside the brain featuring an interactive probe containing structures acquired from fMRI, DTI and various additional MR imaging modes. Uncertainty in the fMRI and DTI data is revealed using uncertainty borders and a different rendering style. Furthermore, they provide a cylindrical access path projection representing the distance to the structures at risk along the planned path. A close-up view of the tumour allows a more detailed view on the area that the surgeons are planning to resect.

Serra *et al.* developed a multi-modal pre-operative neurosurgical planning system designed for use with a mirror-based virtual reality system workbench [SKG*98]. They render CT, MRI and MRA scans using 3D textures and allow the user to interact with the volumes using a tracked 3D pointer. Neubauer *et al.* proposed a surgical simulation application for endonasal transsphenoidal pituitary surgery, which is a minimally invasive endoscopic procedure [NMW*04]. They employ CT and MRI to simulate this endoscopic procedure for training and pre-operative planning purposes. They used CT for skull anatomy, MRI for the tumour, optical nerve and pituitary gland and contrast-enhanced CT and MRI to highlight the internal carotid artery. They provide interactive threshold adjustment to adjust the surface visualizations.

For planning neurosurgical procedures, Beyer *et al.* presented a seminal paper on multi-modal medical visualization that illustrates volumes such as CT, MRI, fMRI, PET and digital subtraction angiography (DSA) [BHWB07]. They propose a skull peeling algorithm that can automatically remove an occluding bony area to reveal the underlying brain. Furthermore, they developed a masked-based approach to show multiple modalities concurrently and a rendering technique to render binary segmented objects with a smoothed ap-

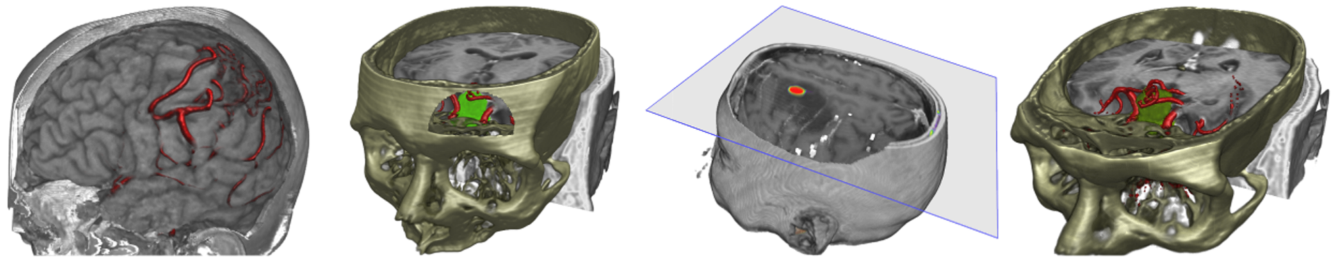


Figure 19: *From left to right: skull peeling, multi-volume rendering of segmented data [green: tumour (MRI), red: vessels (MRA), brown: skull (CT)], multi-volume blending [black/white: brain (MR), red: metabolic active part of tumour (PET)] and perspective volume rendering for simulating keyhole surgery [BHWB07].*

pearance when available (see Figure 19). Within masked parts of the volume, different datasets are rendered, each with their own transfer function settings. Joshi *et al.* presented interaction techniques in a neurosurgical planning application that includes stereotactic navigation [JSV*08]. They visualize MRI, fMRI, DTI and SPECT in a visualization that allows the user to crop volumes using an interactive line widget. Kin *et al.* developed a neurosurgical planning tool specifically focussing on brainstem malformations in which they fuse MRI, CT and 3D rotational angiography together [KNS*12]. They mainly rely on combining multiple surface reconstructions of the individual modalities, which demands a significant amount of pre-processing time in manually segmenting important structures.

Bock *et al.* recently presented a tool for planning and guiding DBS interventions by fusing multi-modal data that include uncertainty regions from the acquisition process [BLE*13]. In order to guide these procedures, CT and MRI are fused and visualized integrated with results from microelectrode recordings (MER), which measure the electric field in the brain intra-operatively. Their tool features a planning, recording and placement phase in which the corresponding steps of the intervention can be performed (see Figure 20). In the area of neurosurgical planning, Rieder *et al.* proposed a multi-modal visualization of intra-cerebral pathological tissue [RSHP08]. They use multiple MRI sequences [T1, T1ce (contrast enhanced), T2, FLAIR] as the input for their visualization application and perform clustering to determine pathologic regions. Next, they blend these pathologic regions with the anatomical context information using an automatically calculated transfer function. Furthermore, they propose an automatic cutting tool and brain peeling to reveal hidden structures of interest.

Weiler *et al.* dealt with neurosurgical planning for treatment of AVMs in the brain [WRD*11], an example of which can be seen in Figure 21. In these procedures, a precise identification of the arteries and veins is crucial to understand the complex inflow and outflow in these vascular pathologies. They combine several differently weighted MRI scans, such as T1-weighted images with and without contrast agent, arterial time-of-flight (TOF) and MR venography (MRV), into a single multi-volume visualization to facilitate understanding of the lesion's angio-architecture. To prevent clutter, they propose a focusing technique, based on the distance to a point of interest, which allows the user to attenuate importance using transparency and saturation manipulation for structures outside the region of interest. Navkar *et al.* developed visualization tools for planning neurosurgical interventions with straight access, such as

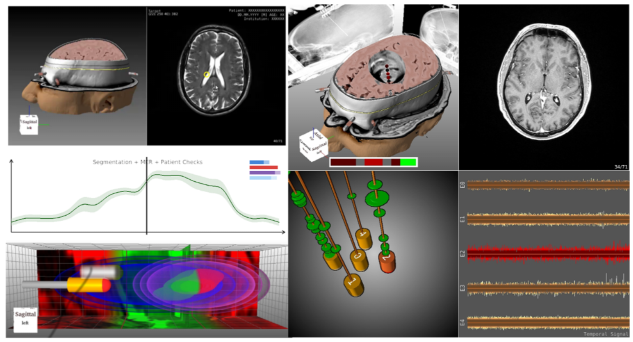


Figure 20: *The DBS planning phase in the top left, recording phase on the right and the placement phase in the lower left [BLE*13].*

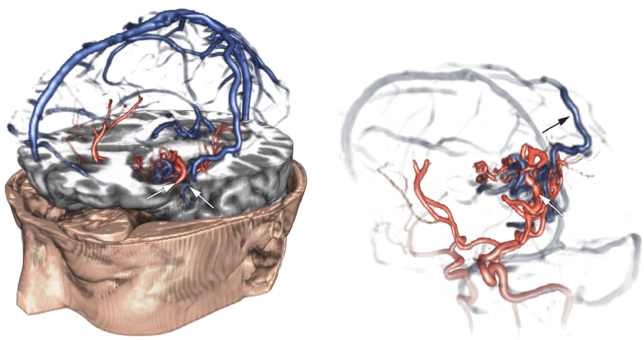


Figure 21: *Visualization of neurovascular anatomy for treatment planning of AVM surgery with context (left) and focused on vascular structures only (right), based on MR-venographies and T1-weighted MRI [WRD*11].*

biopsies, DBS and ablation of brain lesions [NTS*10]. For this, they generate various access maps based on vascular structures on the surface of the skin of the patient's head for guidance in selecting a safe entrance point.

The visualization of fibre tracts from DTI scans is an active research area. Enders *et al.* proposed to visualize white matter tracts reconstructed from DTI with wrapped streamlines [ESM*05]. They generate surfaces that wrap around the convex hull of fibre bundles for a more intuitive representation of tracts and combine this with anatomical information from a T1-weighted scan. Merhof *et al.*

Table 1: *Table of references sorted according to the application type (Type), area (App), and to the acquisition scanners (hybrid scanner, single scanner and multiple scanners). It is stated if any segmentation (Seg) is needed, if the approach was evaluated (qualitatively (Ql), quantitatively (Qt), with domain experts (D) or non-domain experts (N) or the performance (P), and what types of image modalities are used. The visualization techniques that are used are mentioned, subdivided into cutaways (CA), ghosted view (GV), focus-and-context (FC) and illustrative visualization (I-Vis).*

References	Type	App	Scanner	Seg	Eval	Image Modality							Vis technique			
						CT	MRI	fMRI	DTI	PET	SPECT	US	CA	GV	FC	I-Vis
[DHS*13]	Res	Vasc	Hybr	✓	QlD	✓	✗	✗	✗	✓	✗	✗	✗	✗	✗	✗
[RHR*09]	Res	Vasc	Hybr	✗	QlN	✓	✗	✗	✗	✓	✗	✗	✗	✗	✓	✗
[ESM*05]	Res	Neuro	Mult	✓	✗	✗	✓	✗	✓	✗	✗	✗	✓	✓	✓	✗
[vDMvLB12]	Res	Neuro	Sing	✗	QlD	✗	✓	✓	✗	✗	✗	✗	✗	✓	✓	✗
[JNM*09]	Res	Neuro	Sing	✗	QlN	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
[NOE*10]	Res	Neuro	Sing	✗	QtN	✗	✓	✓	✗	✗	✗	✗	✓	✗	✓	✗
[RTF*06]	Res	Neuro	Sing	✗	QtP	✗	✓	✓	✗	✗	✗	✗	✓	✓	✓	✗
[SZV01]	Res	Neuro	Sing	✓	QlD	✗	✓	✓	✗	✓	✓	✗	✗	✗	✗	✗
[SZP*97]	Res	Neuro	Mult	✓	QlD	✗	✓	✗	✗	✗	✓	✗	✗	✗	✗	✗
[JKE*13]	Diag	Onco	Hybr	✓	QtP	✓	✗	✗	✗	✓	✗	✗	✗	✓	✓	✗
[KEF07]	Diag	Onco	Hybr	✗	✗	✓	✗	✗	✗	✓	✗	✗	✗	✓	✓	✗
[LSPV15]	Diag	Onco	Hybr	✗	QlD	✓	✗	✗	✗	✓	✗	✗	✓	✓	✓	✓
[VNØ*08]	Diag	Onco	Mult	❍	QlN	✓	✗	✗	✗	✓	✗	✓	✓	✗	✓	✓
[HSF*08]	Diag	Cardio	Mult	✓	QtD	✗	✓	✗	✗	✗	✗	✗	✗	✓	✗	✗
[OKG*06]	Diag	Cardio	Mult	✓	✗	✓	✓	✗	✗	✗	✗	✗	✗	✓	✗	✗
[TBB*07]	Diag	Cardio	Mult	✓	✗	✗	✓	✗	✗	✗	✗	✗	✗	✓	✗	✗
[KGS*14]	Diag	Cardio	Mult	✓	QtD	✓	✗	✗	✗	✗	✓	✗	✗	✓	✓	✗
[BHWB07]	Trea	Neuro	Mult	❍	QlD	✓	✓	✓	✗	✓	✗	✗	✓	✗	✓	✗
[BBM*07]	Trea	Neuro	Sing	✓	QlD	✗	✓	✓	✓	✗	✗	✗	✗	✓	✓	❍
[BLE*13]	Trea	Neuro	Mult	✓	QlD	✓	✓	✗	✗	✗	✗	✗	✓	✓	✓	✗
[BJH*09]	Trea	Neuro	Sing	✓	✗	✗	✓	✓	✓	✗	✗	✗	✓	✓	✗	✓
[DPL*11]	Trea	Neuro	Sing	✓	QlD	✓	✓	✓	✓	✗	✗	✗	✓	✓	✓	✗
[JBB*08]	Trea	Neuro	Sing	✓	QlD	✗	✓	✓	✗	✗	✗	✗	✓	✓	✗	✓
[JFS*00]	Trea	Neuro	Sing	✓	QlD	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
[JSV*08]	Trea	Neuro	Mult	✓	QlD	✓	✓	✓	✗	✗	✓	✗	✓	✗	✓	✗
[KNS*12]	Trea	Neuro	Mult	✓	QtD	✓	✓	✗	✗	✗	✗	✗	✗	✓	✗	✗
[MSE*06]	Trea	Neuro	Mult	✗	QtP	✗	✓	✗	✓	✗	✗	✗	✓	✗	✓	✗
[NTS*10]	Trea	Neuro	Sing	✓	QlD	✗	✓	✗	✗	✗	✗	✗	✗	✗	✓	✗
[NMW*04]	Trea	Neuro	Mult	✓	QlD	✓	✓	✗	✗	✗	✗	✗	✗	✓	✗	✗
[RRRP08]	Trea	Neuro	Sing	✓	QlD	✗	✓	✓	✓	✗	✗	✗	✓	✓	✗	✗
[RSHP08]	Trea	Neuro	Mult	✗	✗	✗	✓	✗	✗	✗	✗	✗	✓	✗	✓	✗
[SKG*98]	Trea	Neuro	Mult	✓	Ql/QtD	✓	✓	✗	✗	✗	✗	✗	✓	✗	❍	✗
[WRD*11]	Trea	Neuro	Sing	✓	QlD	✗	✓	✗	✗	✗	✗	✗	✓	✗	✓	✗
[NRS*14]	Trea	Radio	Sing	❍	Ql/QtD	✗	✓	✗	✗	✗	✗	✗	✗	✗	❍	✗
[SFNB14]	Trea	Radio	Hybr	✓	✗	✓	✗	✗	✗	✓	✗	✗	✓	✓	✓	✗

proposed a new visualization technique for white matter tracts using triangle strips and point sprites [MSE*06]. Their novel DTI hybrid rendering approach speeds up the rendering process and can then be combined with DVR of anatomical data to provide additional information for surgical planning. For an overview of these visualizations, we refer to a survey by Tobias Isenberg on illustrative visualization techniques for diffusion-weighted MRI tractography [Ise15].

6.3.2. *Radiotherapy*

Radiotherapy planning is generally based on CT, MRI and PET/CT scans. These volumes are used to define target areas for radiation and also organs at risk that should not receive high radiation. Especially for target areas such as chest and upper abdomen, which move strongly due to breathing, the recent possibility to acquire 4D PET/CT data opens the possibility to capture and integrate the movement of tumours into the radiation target volume definition, building the basis for the dose calculation. In contrast to many other diagnostic and treatment planning procedures that occur under severe time pressure, radiation treatment planning is advanced and time-consuming. Thus, advanced multi-modal visualization techniques along with appropriate interaction techniques to explore and focus are required to convey this information.

Schlachter *et al.* [SFNB14] showed that 3D and 4D visualization of images, combined with delineated regions, and the calculated dose (also available as volume dataset) complements the common slice views (see Figure 22). This provides a fast overview over the spatio-temporal configuration of all delineated areas and the related dose distribution resulting finally in a faster quality checks of the radiation plan.

MRSI data provide metabolic information that quantifies the concentrations of multiple brain metabolites, such as choline and

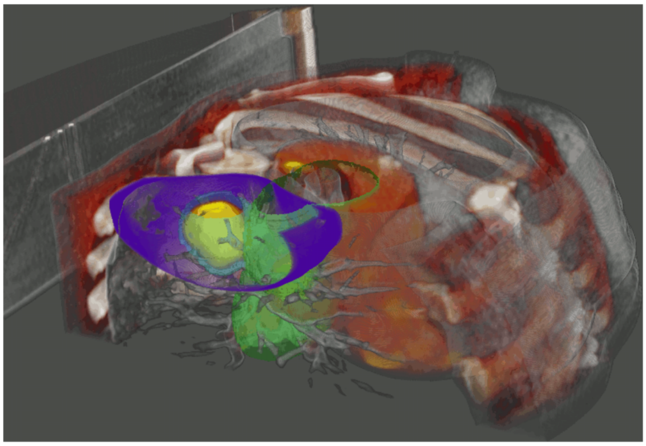


Figure 22: *Fusion visualization of 4D PET/CT with segmentation and dose information combined with clipping [SFNB14].*

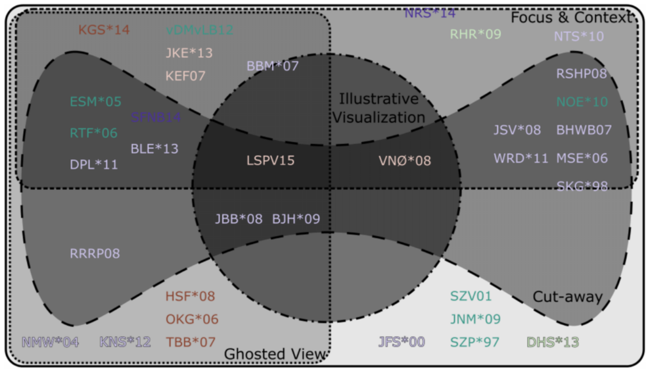


Figure 23: *A Venn–Edwards diagram of the references categorized according to the applied visualization techniques. The colour of the references corresponds to the application-type colours: vascular research, neuroscience, diagnostic oncology, diagnostic cardiology, neurosurgical treatment planning and radiotherapy planning.*

creatine, per voxel. Currently, MRSI is only performed in a clinical research context. In the work by Nunes *et al.*, MRSI data are fused with multi-modal radiology imaging in an integrated visual analysis system aimed at radiotherapy treatment [NRS*14]. They linked the medical imaging framework MITK and the general-purpose data exploration tool ComVis to analyse, relate and visualize MRSI data together with multi-modal images.

6.4. Discussion

An overview of all papers according to the application type and application area can be found in Table 1. Here, we stated if any segmentation is needed for processing the date in order to visualize it, which is important to estimate the amount of pre-processing an application requires. We mention which type of evaluation (if any) was performed to verify the utility of the applications. For this, we distinguish between quantitative (Qt) and qualitative (Ql) studies with domain experts (D), non-domain experts (N), or if the performance was tested (P). Furthermore, we mention the image modalities visualized and describe the visualization techniques that are applied for the visualization of the multi-modal medical data. Additionally, we have composed a Venn–Edwards diagram of all application papers categorized according to the visualization techniques used and the application type in Figure 23.

From the table, we can see that a fair amount of work has been done on neurosurgical treatment planning, as well as work on guidance. Not much work has been done yet on radiotherapy planning, while this field especially uses multi-modal data and is in need of suitable visualization methods.

There has only been one visualization application paper combining ultrasound with another modality, although ultrasound has great potential and benefits that can be complimentary to other modalities, such as the ability to provide real-time information. The limited field of view and noise in ultrasound data could be alleviated by combining it with additional modalities, and could be of value also in, for instance, biopsy guidance. SPECT is involved only in cardiac diagnostic and neuro-science and neuro-surgical planning applications. A popular modality combination for both vascular research and oncologic diagnosis is PET/CT, which is used in all the application papers we listed. Due to the nature of MRI, fMRI and DTI data, these modalities are often involved in both neurosurgical treatment planning and research. For obvious reasons, fMRI is completely neuro-specific, but DTI is also clinically applied so far mainly in neurological contexts.

While the visualization techniques used per application area vary too much to make strong conclusions based on the limited number of samples, it is clear that ghosted views are often employed for research papers intended to support diagnostic purposes (see Figure 23). Furthermore, cutaways are most successfully applied to neurosurgical planning, which makes sense due to the nested anatomical and pathological structures involved and the need for exact access path planning through the skull. There are five papers not employing smart visibility or illustrative techniques, mainly in a research context.

In most works, qualitative evaluations with domain experts are presented, but quantitative evaluations as well as more elaborate clinical studies are often still needed. Furthermore, our overview revealed that only a few works applied illustrative visualization techniques [LSPV15, BJH*09, JBB*08, VNØ*08]. However, the application of illustrative visualization technique seems to be promising [TIP05, Law15] and we see a potential to use these techniques for further research on multi-modal medical visualization. In multimodal medical visualizations, there are often many overlapping and nested structures, which causes occlusion problems that the abstraction in illustrative techniques can help alleviate. However, the segmentation required often limits the clinical uptake. It might also be helpful to employ novel focus-and-context techniques, by defining one modality as the focus and the other(s) as the context.

7. Conclusion and Future Challenges

For many techniques described in this survey, it is not clear how they fit in clinical workflows, how much additional and relevant information they provide, and whether this justifies a potentially larger effort, e.g. due to the necessity to segment structures or adjust (2D) transfer functions.

Dealing with medical imaging data involves uncertainty in the form of imaging errors, for instance, resulting from noise, field bias, patient motion or imaging artefacts. Additionally, processing errors may occur due to errors in the segmentation or registration process. When visualizing multi-modal datasets resulting from combining acquisitions of multiple scanners, additional care has to be taken to visualize the uncertainty resulting from these processing errors in the registration process. This is a challenging and so far unsolved research challenge [RPHL14]. When visualizing combined data, the reliability of the result needs to be clearly conveyed. One possible extension to medical multi-modal visualization solutions would be to incorporate the uncertainty in the visualization, which leads to the question of how to display this uncertainty without distracting the expert. This results in visualization approaches that cope with the problem of showing different types of information combined, e.g. CT, PET and the registration error. This might be an interesting question for further consideration in the future.

Besides the challenge of representing uncertainty in an appropriate way, existing multi-modal visualization techniques need to be better evaluated and compared. On the one hand, evaluations that consider effectiveness in specific medical tasks are needed. On the other hand, perception-based evaluations are essential, e.g. to understand how effective certain emphasis techniques actually are, how well users could discriminate values with certain colour scales (used as overlays) and how accurate they can locate functional abnormalities. Furthermore, this survey shows that different illustrative visualization techniques can be employed to cope with the challenge of showing different data structures. Also here, more evaluations are needed that analyse if one technique is preferred over other approaches for certain scenarios. This question does not only concern user preferences, but also effectiveness of the visual encoding. For example, one can imagine an evaluation involving a high amount of physicians tasked with identifying and staging a tumour scanned with, e.g. PET/CT. Then, various visualization techniques could be employed and the identification time could be measured.

The existing techniques are spread over many research prototypes and a few commercial solutions. It is thus very difficult to compare them. A framework that integrates at least the most commonly used techniques and flexible parameterization options would be very valuable. A comparison also benefits from benchmark tasks and data. A first step in this direction was the IEEE Vis. 2010 contest on multi-modal brain data for neurosurgery planning. A few more such tasks, e.g. in cardiology, would be beneficial.

We have seen a multitude of visualization techniques. Interestingly, these are exclusively techniques that were developed first for displaying single datasets and then adapted and refined, typically for use with two modalities. An open question is whether truly multi-modal techniques can be developed, or techniques that go beyond combining two modalities. Multi-modal visualization obviously benefits from multiple views. More research is necessary to understand which views are essential, how flexible viewing configurations should be and which synchronization/coordination techniques are needed.

The visualization of single medical datasets may benefit from automatic viewpoint selection, i.e. choosing a good initial view on a dataset as starting point for further exploration [BS05, MNTP07, KBKK07, KBKG08, RCL16]. Measures of visibility, size of objects and viewpoint stability are employed for the viewpoint selection. Automatic viewpoint selection is also promising for multi-modal data visualization and requires careful adaptation of measures and application to selected case studies. Showing one viewpoint may be helpful to let the user focus to the specific region, but it might be even more helpful to let the camera follow a path. In this way, the user may get insights into surrounding regions and to acquire a better spatial feeling with regard to, for example, distance to surrounding structures. Also, the user interface must be considered to enable a physician to specify what is important as input for an algorithm.

Neurosurgery is among the most advanced user communities in this field, while other disciplines like radiotherapy are not yet exploiting the full potential of visualization techniques available today to support therapy planning and monitoring. We believe that there are many applications in neurosurgery because of the relatively easy and reliable registration process, which can be automated, as well as specific application demands. First, CT and MRI contribute a significant amount of relevant and complementary information, while in lung surgery, for example, most relevant information can be extracted from CT data. Second, neurosurgery has much higher accuracy demands compared to any type of abdominal surgery. A few millimetres in abdominal surgery usually do not matter, while in neurosurgery 2 mm may be a lot.

Challenges also appear in case when the input does not consist of surface meshes. For volumetric data, some visualization techniques are more challenging than when applying them to surfaces. Feature lines are mostly defined on surfaces, but some methods can also be applied on volumetric data. Burns *et al.* [BKR*05] extended the suggestive contours to volumetric data. They also extract the lines as objects, and with this, the lines could also be stylized. Kindlmann *et al.* [KWTM03] visualized ridges and valleys depending on curvature values. With an adapted transfer function, these lines can be highlighted, which is similar to the approach by Lawonn *et al.* [LSPV15]. In contrast to feature lines, hatching approaches were also applied to volume datasets [DCLK03, CD05, PVW08]. Mostly particles or points are placed in the dataset on a specific isovalue, and then the points are traced along the principle curvature directions. Due to the challenging character of feature lines, these techniques were not commonly applied to multi-modal data visualization so far. Although its potential was shown to illustrate surfaces [Law15] more work need to be done in this field.

Developing efficient and effective visualization methods with real impact on daily clinical or research routine of potential users requires a highly interdisciplinary effort fusing knowledge from physicians, visual computing specialists, human computer interaction (HCI), imaging and image analysis specialists. This becomes even more important with the increasing availability of new imaging modalities that can be fused with imaging pipelines delivering sets of highly heterogeneous data at different scales. A deep understanding of this data and its application context is necessary to generate useful results; on the other hand, technical skills are getting more and more important, as the amount of data to be processed increases tremendously. As a consequence, multi-modal visualization will be even more interdisciplinary than it has been ever before.

8. Summary

We have presented a survey of the current state of the art in medical multi-modal visualization. We introduced relevant medical imaging modalities and acquisition techniques as well as the associated visualization challenges. Afterwards, we examined the current clinical workflow for the exploration and analysis of multi-modal medical modalities. We summarized the requirements in designing a visualization technique to maximize the insights into relevant details in the depiction of multi-modal medical data.

Subsequently, we highlighted the most common visualization techniques that support this visualization problem. These techniques need to incorporate heuristics for assessing the importance of information and emphasis techniques to adapt the importance. For this reason, smart visibility approaches, including focus-and-context techniques, ghosted views and cutaways are highly relevant for visualizing multiple volumes. While these techniques are frequently used in visualization research, they are not part of any commercial solution or available in radiology workstations. This is probably because these techniques require time-consuming pre-processing and are unfamiliar to the physicians.

Rendering multiple volumes is an associated research challenge for which many approaches have been developed. Furthermore, special interaction techniques have been designed for exploring multi-modal datasets, which can be as important in providing insight in multi-modal data as rendering refinements.

In the main part of our survey, we provided an overview of 35 visualization application papers. We defined the scope of the paper by focusing our survey on multi-modal medical visualization applications associated with research, diagnosis and treatment planning or guidance. Within these categories, we found that the main application areas were related to oncology, cardiology, radiotherapy and neurology. We summarized our findings in a table featuring the three aforementioned categories, a further subdivision according to the medical application domain, whether pre-processing is required in terms of segmentation, image modalities used and visualization techniques employed. We concluded from the table which application areas are active, upcoming or sufficiently researched. While a fair amount of work has been done on neurosurgical planning, radiotherapy planning seems to be a rising field with many opportunities for interesting research, and the same holds for combining ultrasound with other modalities.

Most developed techniques were extended from single modality techniques, while truly multi-modal techniques have yet to be developed. With the increase in the amount of data acquired and new modalities being brought into clinical practice, multi-modal medical visualization remains a promising research area for future developments.

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