Endovascular interventions proceeded under contrast agent and radiation sparing using navigation and imaging techniques for holographic visualisation

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This review provides an overview to current endovascular techniques which may reduce the amount of contrast agents and radiation exposure to patient and staff. One integral part for the success of endovascular procedures is innovative and improved vascular imaging. A major challenge during these interventions is visualizing the position and orientation of the catheter being inserted. This is typically achieved by intermittent X-ray imaging and contrast agent application. While endovascular techniques are improving, imaging during the procedure is still dependent on contrast agents and X-Rays with their known disadvantages. Looking at current developments towards radiation-free localization of endovascular tools, the visualization and proper integration of this spatial information will become a key technology.

After an extensive literature review of pathophysiology and clinical side effects of contrast agents and radiation exposure, we describe established procedures added with current experimental work to reduce these well known side effects in endovascular procedures.

Based on the ALARA-principles modern angiography systems show optimized technical settings to deliver the best image quality at low radiation levels, such as optimal collimation, flat panel detector technology, pulse mode, auto exposure settings, low-dose modes and anti-scatter grids. Carbon dioxide (CO₂) angiography, contrast-enhanced ultrasound (CEUS) imaging, appropriate C-arm angulation for optimal visualization have become standard procedures in large vascular centers. Optical fiber technologies combined with navigation techniques, augmented reality and holographic visualization techniques are under current experimental development. These techniques seem to have the potential as a disruptive technology in future endovascular therapy.

Advanced image application and upcoming techniques focus contrast agent and radiation exposure and even some show a disruptive character. The navigated visualization of vessels and spatial position and endovascular tools during interventional procedures will probably become a key technology in future.

Introduction

Cardiovascular diseases are the most common cause of death in industrialized countries. This includes coronary, neurological, abdominal and peripheral vessels. For example, globally more than 200 million people are currently suffered by peripheral occlusive disease (PAD)¹. Over the last decades endovascular treatment of vascular diseases became extremely important based on an exponential increase of endovascular materials and techniques. Nowadays these minimal invasive procedures are suitable to nearly all vessel systems of the human body and are proceeded for various indications by different specialties, like Cardiology, Radiology,
Vascular Surgery, Neuroradiology, Dermatology or Angiology. One integral part for the success of endovascular procedures is innovative and improved vascular imaging. A major challenge during these interventions is visualizing the position and orientation of the catheter being inserted. This is typically achieved by intermittent X-ray imaging and contrast agent application. This method was first introduced in humans about 90 years ago, in the 1920s, and the basic technology used in our days is still very similar. While endovascular techniques are improving, imaging during the procedure is still dependent on contrast agents and X-Rays with their known disadvantages. Looking at actual development trends towards radiation free localization of endovascular tools, the visualization and proper integration of this spatial information will become a key technology.

Contrast agents and radiation

Contrast agent

Most endovascular procedures are performed by using iodinated contrast agents to visualize vascular structures, because of its high-contrast density. Next to allergic reactions, a very important unwanted effect of the use of contrast drugs is acute kidney injury (AKI), which is a sudden decrease of renal function due to renal damage. AKI secondary to contrast drugs is called contrast-induced AKI and it is actually an iatrogenic AKI. After intravascular injection, the drug is diluted in the bloodstream (this allows the visualization of vessels of liver, spleen, pancreas, and kidneys, etc) and immediately distributed throughout the extracellular fluid. Being poorly bound to serum albumin, the contrast drug is freely filtered by renal glomeruli and excreted by the kidneys. Contrast drugs have been shown to cause the following changes: renal vasoconstriction, resulting in a rise in intrarenal resistance (decrease in renal blood flow and glomerular filtration rate and medullary hypoxia); epithelial vacuolization and dilatation and necrosis of proximal tubules; potentiation of angiotensin II effects, reducing nitric oxide (NO) and causing direct constriction of descending vasa recta, leading to formation of reactive oxygen species in isolated descending vasa recta of rats microperfused with a solution of iodixanol; increasing active sodium reabsorption in the thick ascending limbs of Henle’s loop (increasing O2 demand and consequently medullary hypoxia); direct cytotoxic effects on endothelial and tubular epithelial cells (decrease in release of NO in vasa recta); and reducing cell survival, due to decreased activation of Akt and ERK1/2, kinases involved in cell survival/proliferation. A huge amount of patients suffered by vascular diseases show already impaired renal function. It has been reported that in 10% of patients with renal failure exposed to contrast drugs for coronary angiography, a severe oliguric acute renal failure occurred that led to dialysis or death. Some studies suggest that about 40% of all patients with abdominal aortic aneurysm already have impaired renal function. Administration of contrast medium may cause renal function to deteriorate in up to one third of patients. Postoperative impairment of renal function is the third most common complication following EVAR and is a predictor of increased mortality. The main risk factor for renal impairment with endovascular procedures is the use of nephrotoxic contrast medium for angiographic navigation. Considerably more contrast agent is administered as the anatomical conditions become more complex.

Radiation

X-ray imaging is based on the seemingly simple physics of the interaction of x-rays with matter. X-rays are both electromagnetic waves and particles (photons) that move along straight lines in a vacuum. They are powerful enough to deeply penetrate in matter and are able to cross it in certain conditions. A shadow image is seen because certain parts of the body are more transparent to x-rays than others. In all cases, some x-rays are absorbed (entirely or partially) by the body. This absorption effect is called the radiation dose, and therefore, it is inherent to x-ray imaging to supply a radiation dose to the patient. However, patients, as well as operators, are exposed to significant radiation doses during endovascular procedures. The impact of radiation exposure from endovascular procedures has been described previously, and can be divided into deterministic and stochastic effects. A threshold of 2 to 3 Gy is commonly considered to be at risk for deterministic effects, such as skin injuries. In recent studies, radiation exposure during endovascular aortic repair (EVAR) was estimated to cause deterministic effects in 30% of the procedures. Stochastic effects...
of radiation due to repetitive exposure of the staff may induce cancer or cataract, years or decades after the procedures\(^1\). The probability of these effects increases with the cumulative radiation exposure. The dose area product (DAP in Gy cm\(^2\)) accumulated during the procedure is linked to the stochastic effect and can be converted in a first approximation to the effective dose (in Sv) using a conversion factor\(^4\). Digital subtraction angiography (DSA) runs of the abdomen and pelvis, especially with the C-arm in an oblique position, have been identified as contributing to a significant radiation exposure and constitute a considerable proportion of the cumulative dose area product during EVAR procedures. Especially complex endovascular procedures like EVAR or transcatheter aortic valve implantation (TAVI) leads to relevant radiation exposure to the patient and staff. For example in fenestrated Aortic Stentgraft procedures (fEVAR) radiation time may rise up to two hours\(^1\) (Figure 1). All patients undergoing endovascular procedures and operators performing them face possible short- and long-term risks from radiation exposure\(^16\).

Established techniques in reducing contrast agent and radiation in endovascular therapy

The risk-benefit ratio of x-ray use in medical practice has to be considered for each patient and procedure in order to obtain sufficient image quality at a minimum dose while allowing for safety and efficacy. This concept is referred to as the “as low as reasonably achievable” (ALARA) principle\(^8\). To achieve this goal, different strategies are established and presented below. However, when available, non–x-ray procedures need to be considered.

X-rays are undetectable by the human eye, therefore optimized room setup is required for passive protection, as well as dose awareness and alerts are needed to help to protect the patient, the staff and the operator. Because the main source of passive radiation to the operator is scattered radiation, distance and shielding are simple but important methods to reduce exposure. Levels of scattered radiation decrease by the inversed squared distance and therefore longer distance are helpful to decrease occupational exposure. Because scattered radiation is highest at the entrance point of the beam into the patient and most of the upward x-ray energy is absorbed by the patient, radiation levels are higher under the table. Consequently, the tube should always be positioned under the table to avoid the highest scattered radiation being directed at the operator’s head and ceiling-mounted shields need to be used\(^17\). To monitor patient exposure, modern interventional fluoroscopy systems are capable of displaying a number of metrics related to patient dose, including the fluoroscopy time, the DAP, and the cumulative Air kerma (CAK, in Gy; kerma refers to the kinetic energy released per unit mass). However, these metrics do not directly measure patient dose, but are intended to provide information in real time to allow...
the physician to decide to stop the procedure or change strategy. To monitor the occupational exposition of the staff passive dosimeters are common. As opposed to a passive dosimeter, active dosimeters provide a direct display of the accumulated dose and dose rate, as well as some additional functions, such as alarm threshold settings for dose or dose rate values. Active dosimeter are recommended because they allows the medical staff to adjust their behavior and avoid unnecessary occupational radiation exposure. Longitudinal dose analysis due to collecting and storing dose data allows continuous self-evaluation and helps to manage and control the risk to patients and staff in the long term. Dose information tracking systems (eg, DoseWatch, GE Healthcare) are currently available.

Next to dose monitoring and awareness, modern angiography systems show optimized technical settings to deliver the best image quality at low radiation levels, such as flat panel detector technology, pulse mode, auto exposure settings, low-dose modes and anti-scatter grids18. Moreover Good Radiological Practice need to be known and constantly performed by the operator. The time on the foot pedal should be reduced to a minimum. DSA is commonly used for diagnosis or documentation purposes but requires substantial additional radiation exposure compared with standard fluoroscopy. Therefore, the use of fluoroscopy must be preferred and DSA runs limited where possible16. Reduction of the field of view (FOV) by optimal collimation on the area of interest allows significant dose reduction (proportional to the image reduction). In addition, magnification increases the dose, but can be avoided by using large display monitors. As already mentioned angulations should be limited because it increases staff exposure and decreases image quality8.

Renal dysfunction after endovascular aortic aneurysm repair is an increasingly recognised problem. Carbon dioxide (CO2) angiography has been used to limit the risk of contrast nephrotoxicity during endovascular procedures. While iodinated contrast agents are radio-opaque liquids, CO2 is a radiolucent, highly compressible gas. Iodinated contrast agents mix with the blood within the vascular tree to produce an image; CO2 displaces the blood within the vascular tree to produce a difference in density between the vessel and the surrounding soft tissue. Theoretically, injection of a gas into a blood vessel can lead to a fatal “vapor lock” of the pulmonary artery as it happens in air embolism. The volumes normally used for medical imaging are rapidly eliminated without any physiological effects. The use of CO2 above the diaphragm is, however, not recommended because of disruption of the blood brain barrier. The commonest problem reported in the literature is unsatisfactory demonstration of the target vessels, e.g. renal arteries during EVAR procedure19.

New and upcoming techniques of imaging and navigation during endovascular procedures

**Contrast medium-enhanced ultrasonography**

Contrast-enhanced ultrasound (CEUS) imaging using nonnephrotoxic sulphur hexafluoride microbubble contrast is a novel imaging modality that accurately identifies and characterizes endoleaks during EVAR follow-up. A recent study suggested that intraoperative 3D CEUS imaging can accurately identify the renal arteries and endoleaks immediately after stent graft deployment. Furthermore, 3D CEUS imaging may detect and characterize endoleaks not seen on uniplanar angiography, including clinically important type I endoleaks, and has advantages over 2D CEUS imaging in inflow vessel identification and image manipulation20. When combined with the use of CO2, 3D CEUS can provide satisfactory completion imaging and reduce the exposure to both radiation and nephrotoxic contrast during EVAR16. Other studies on CEUS have shown reductions of up to 30% in fluoroscopy time and of more than 50% in the use of contrast agents in EVAR. Besides the initial outlay for a suitable ultrasound scanner with special software and the long learning curve and experience required, the main disadvantages
of this procedure are the limitations imposed by tympanites, obese patients, complex anatomy and severe vascular calcification. Ultimately, this procedure cannot be used adequately in every patient.

**Preoperative image analysis and planning**

Accurate planning of the endovascular procedures (especially in EVAR procedures) with preoperative imaging analysis on a three-dimensional (3D) workstation allows to calculate an appropriate C-arm positions. The old-fashioned "diagnostic" run at the beginning of interventional procedures is no longer required. Our study group showed significant reduction in radiation and contrast medium exposure due to pre-operative simulation of the appropriate C-arm angulation for ideal visualisation of landing zones during EVAR procedures using 3D computed tomography angiography (CTA) post-processing software. This method has the potential to reduce the amount of radiation and the volume of contrast medium during other interventions.

Another upcoming method for optimizing the procedures' planning, especially in complex cases, may be 3D printing of patient specific vascular models. Even if there is no clear evidence at the moment, some authors and companies suggest simulation of complex endovascular procedures (e.g. fenestrated EVAR) to patient specific vascular models before patient application. Next to the major aim to avoid misplacement of stent grafts, other secondary issues like reduction of radiation or contrast agent exposure may feasible by using this method. Following the trends in precision medicine, 3D printing in EVAR procedures seems to be valuable for further research (Figure 2).

**Image fusion**

Advanced imaging applications, such as fusion imaging, are available in most hybrid rooms. Several methods are described to register a 3D volume, either from the pre-operative CT angiography, or from a contrast enhanced cone beam CT acquired during the procedure. Currently the most commercial software systems use a bone tracking principle to overlay pre-operative 3D datasets and intraoperative fluoroscopy to provide a "3D roadmap" during the procedure. The 3D overlay image can be used selectively to confirm the wire path as the target vessel of interest, decreasing the need for DSA during catheterization. At present these advanced techniques are used in EVAR and complex EVAR procedures. DSA is typically reserved for a completion aortogram and/or during difficult vessel catheterizations. Few studies to image fusion techniques reported significantly decrease in radiation and contrast agent exposure, as well as in procedure time during standard and complex EVAR. Integration of these advanced imaging applications appears costly.
and exhausting at first glance, but worthwhile to both, the operator and the patient. However, further investigation of image fusion techniques are necessary and implementation during other endovascular procedures may be useful.

Sensor tracking systems

Experimental investigations on the combination of advanced image application and new hardware sensor techniques appears promising to reduce radiation and contrast agent exposure. Moreover new kinds of visualisation during endovascular procedures are in process.

For several years, fiber-based measurement of the 3-dimensional profiles and shapes of mechanical objects has been the focus of various research groups throughout the world. Conventional electromagnetic (EM) tracking systems, which are favoured in biomedical engineering, are relatively susceptible to interference and are also expensive\(^2\)\(^6\). To locate individual sensors, a transmitter/receiver unit has to be placed immediately next to the patient, which is inconvenient in the confined space of an investigative procedure. All ferromagnetic objects in the vicinity considerably reduce the accuracy of the system. Alternative optical tracking systems based on triangulation have the disadvantages that the field of vision must be clear and navigation within the body is not possible.

The passive measurement of the 3D profiles and shapes of mechanical objects using fiber optic sensors has opened up entirely new possibilities for determining position and navigation in the order of centimetres to micrometres, as well as on the much larger scale of several hundred metres to kilometres. Using precise laser technology, periodic modulations of the refractive index can be written directly into the core as well as the cladding of an optical fibre. In this way, several microscopic optical stretch sensors can be built into a fiber. In addition, deliberate rotational asymmetry of the fiber Bragg grating points can be used to determine the torsion of the optical fibre. Analysis of the expansion and compression data obtained gives a 3D profile of the fiber – and therefore also of the instrument in which the fiber is integrated. In cooperation with Fraunhofer Heinrich Hertz Institute, we already implemented an experimental set-up for further investigations (Figure 3). The fiber unit can be integrated into stentgraft sheaths (through additional drill holes) or conventional catheters. Multimodal registration of the optical fiber thus integrated into the system allows 3D navigation through the 3D vascular model in real time. The actual position in the surgical field is determined using the information from the fiber-Bragg tracking. This is firstly aligned with fluoroscopy, obtained routinely as before, and secondly checked for plausibility. Alignment with the actual position in the surgical field is necessary because of the non-linear deformation of the patient’s

Figure 3: Experimental navigation in a 3D-printed model using fiber-Bragg-technology (Fiberoptic 3D-Shape System, Photonic Concepts, Goslar, Germany)
aorta and soft tissues to be expected during the intervention. Preoperative planning CTA is used for 3D reconstruction of aortic anatomy by volume-rendered segmentation. At the beginning of the intervention the relevant landmarks are matched in real time with the two-dimensional angiographic scene. Conversion into a 3D scene is performed due to appropriate interfaces, and the surgeon can then use the 3D rendering to navigate the instrument (Figure 4). During the intervention, the software continuously registers the position of the fiber which is integrated in the guide-wire, catheter or stent sheath. An additional 3D-screen shows the generated endoluminal view during the whole intervention in real time. Currently this technique was already used to simulate endovascular navigation in patient-specific vascular phantoms in an experimental setting. However, To implement fiber-Bragg navigation further experimental studies are necessary to verify accuracy before clinical application.

Augmented Reality and Holographic Visualization

Next to improved navigation, visualization and integration of spatial information during endovascular procedures will become a key technology. Therefore visualization of vessels by Virtual Reality (VR) and Augmented Reality (AR) is under active research\textsuperscript{27}. A first proof-of-concept study showed an overall positive validation among clinicians, like vascular surgeons, radiologists and thoracic surgeons\textsuperscript{28}. In this study, a real-time navigation framework was developed, which allows a three-dimensional holographic view of the vascular system without any need of radiation in an experimental setting. A vascular phantom model and an AR headset (Microsoft HoloLens) were used to display the vascular structures. Using an EM tracking system, the position and orientation of an experimental wire inside the vessels was displayed. Using extrinsic landmark-based calibrations, the virtual objects are precisely aligned with the real world, resulting in a convincing holographic illusion. The preliminary results of navigated virtual angioscopy are promising (Figure 5). The “virtual angioscope” may improve intraoperative visualization, placement of guide-wires and stents. It may reduces the amount of contrast agents and exposure to X-rays. The prototype also offers the possibility of intervention planning and simulation, which in turn will lead to a reduced learning curve and therefore increased patient safety. 3D holographic visualization may be a disruptive technology.

Figure 4: Virtual Angioscopy based on patient-individualized CTA datasets (Courtesy Fraunhofer MeVis, Lübeck, Germany)

Figure 5: Augmented reality view of the phantom and the registered surface mesh as extracted from the CT scan (blue). The phantom’s vessel tree (yellow) and the landmarks used for registration (red crosses) are clearly visible. The position of the catheter inside the vessels is visualized as a red sphere. This image can be obtained without the application of X-rays or contrast agent. (Courtesy Prof. F. Ernst, Institute for Robotics and Cognitive Systems, University of Lübeck, Germany)
Conclusion

Endovascular treatment features benefits compared to open surgery and indication expanded constantly over the last decades. Current disadvantages of this minimal invasive method are radiation exposure and contrast agent application. Advanced image application and upcoming techniques aim to these problems and even some show a disruptive character. The visualization of vessels and spatial position and endovascular tools during interventional procedures will become a key technology in future.

References