Chapter 12
Radiological Contrast Media and Injector Systems

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12.1 Contrast Medium

12.1.1 Introduction

Since Roentgen discovered X-rays in 1895, they have remained an integral part of medical practice. Medical demands placed on X-ray imaging techniques have necessitated the continual development of the imaging technology; alongside this the need for contrast medium as an integral component of many X-ray procedures has emerged. In 2004, it was estimated that approximately 60 million doses of contrast medium are administered worldwide each year [1].

This chapter will focus on the use of contrast medium (agent) within CT. Specifically, it will attempt to describe the use of intravenous contrast medium and the use of pressure injector delivery systems. Within CT, a positive contrast medium has a wide range of clinical applications. In particular, it allows exquisite detail to be obtained of vascular systems throughout the body along with the demonstration of hypervascular organs such as the liver or kidneys.

Contrast medium is used to assist in the diagnostic accuracy of a variety of radiological tests. Contrast can be defined as the perceived difference between two adjacent structures. Within radiography, contrast can be defined as the difference in optical

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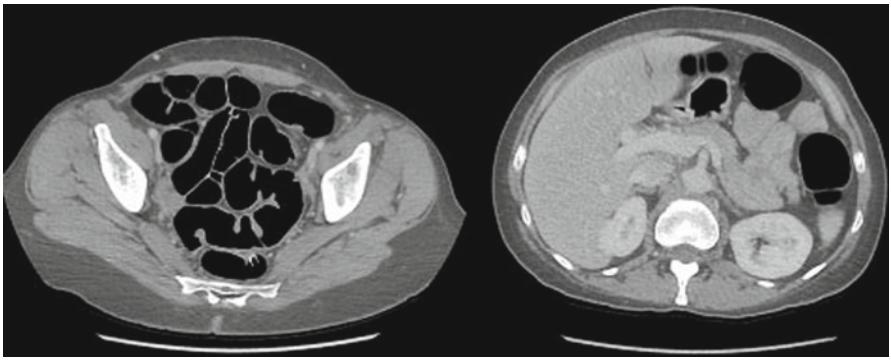

Fig. 12.1 Demonstrating the use of carbon dioxide as part of a CT colonography examination

density in a radiograph that results from a difference in radiolucency or penetrability of the subject [2]. When natural contrast exists between two structures within the body, it can be described as having good inherent contrast resolution. Examples would be between the dense cerebral tissue of the brain and the low-density cerebrospinal fluid found with the ventricles, or within the variety of tissue densities demonstrated within the thoracic cavity when imaging the lung tissue. It is usually the case that differentiation of those adjacent structures can be realized without the need for contrast medium. The primary aim of contrast medium is to increase the differentiation between adjacent structures by increasing the difference in attenuation of the X-rays by an organ or tissue. Soft tissue throughout the body does not sufficiently absorb X-rays [3] and as such inherent contrast between soft tissues can be low. Contrast agents are also useful to help characterize pathology and to demonstrate vascular structures.

Generally speaking, contrast medium is positive – that is, it will produce a higher attenuation value than surrounding tissue. It can also be negative – this will produce a lower attenuation value than surrounding tissue. Intravenous contrast medium is one example of a positive contrast medium. Carbon dioxide or air is an example of a negative contrast agent; this can be introduced into the rectum during a CT colonoscopy examination (see Fig. 12.1). Another commonly used negative contrast agent is water which is often used for CT studies where imaging of the esophagus and stomach is important. The use of negative contrast agents in such examinations allows good demonstration of the gastric mucosa which is often obscured due to artifact from a positive contrast agent.

Figure 12.1 demonstrates the use of negative contrast agent (in this case carbon dioxide as part of a CT colonography examination) which has been used to insufflate the colon. This acts to distend the colon and eliminate haustral folds which could obscure pathology such as a small polyp and also gives the colon a negative contrast allowing excellent visualization of the bowel wall. Note that the image to the right demonstrates the use of positive contrast in the form of intravenous contrast media which can clearly be seen in the kidneys, aorta, superior mesenteric artery, and hepatic portal vein.

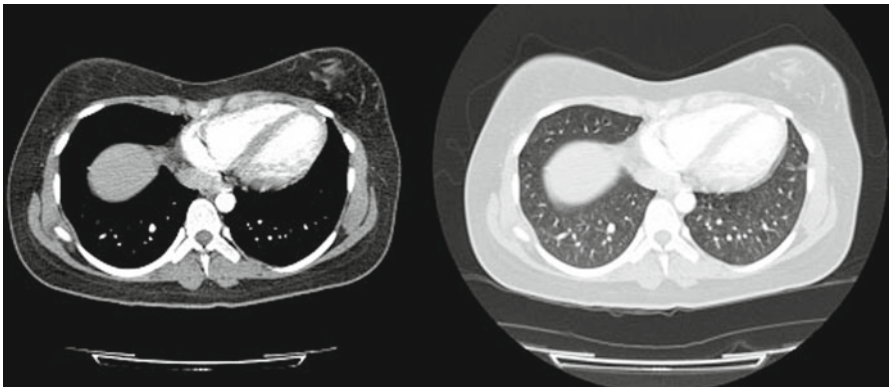

Fig. 12.2 Demonstrating the use of positive contrast in the form of intravenous contrast medium

Figure 12.2 demonstrates the use of positive contrast in the form of intravenous contrast medium. The images form part of a CT pulmonary angiographic study, and as such they have been acquired in arterial phase; the images clearly demonstrate the pulmonary vessels and chambers of the heart. These two images also demonstrate the exceptional inherent contrast properties of the thorax. The lungs have low attenuation as they contain air which acts as a natural negative contrast agent.

Intravenous contrast media are water soluble and iodine based with three iodine atoms being attached to a benzene ring. They can occur as monomers, where the molecules consist of one tri-iodinated benzene ring, or dimers, where the molecules consist of two tri-iodinated benzene rings.

Contrast agents can be divided into ionic or nonionic depending on whether the molecules dissociate in water or not. Ionic contrast agents dissociate into positive and negative ions; no dissociation occurs with nonionic contrast agents.

Contrast can be further divided into high osmolar contrast media (HOCM), low osmolar contrast media (LOCM), and iso-osmolar contrast media (IOCM). HOCM have five to eight times the osmolality of plasma, LOCM have two to three times the osmolality of serum, and IOCM have the same osmolality as blood and cerebrospinal fluid [4].

When a contrast agent is introduced into a vessel, it draws water by osmosis from the surrounding tissues; hence, it exerts osmotic pressure. The osmolality of a contrast agent is dependent upon its dissolved particle concentration. Consequently, as ionic contrast agents dissociate in water, they tend to have a higher osmolality (more particles) than nonionic contrast agents. Generally speaking, HOCM are not tolerated as well as contrast media with an osmolality closer to that of body fluids, for example, blood and cerebrospinal fluid. Higher osmolality is responsible for symptoms such as heat, discomfort, and pain [5].

Contrast media can vary greatly in viscosity and in osmolality. Early contrast media had high osmolalities, and subsequently their use led to more adverse reactions than current media. In further attempts to reduce osmolality, iso-osmolar media were developed, which was only possible with a corresponding increase in viscosity.

Table 12.1 Some of the most common CT contrast media in use today

Trade name	Manufacturer	Pharmaceutical name	Concentrations	Additional information
Visipaque	GE Healthcare	Iodixanol	320, 270	Iso-osmolar, nonionic
Niopam	Bracco	Iopamidol	150, 200, 300, 340, 370	Low-osmolar, nonionic
Omnipaque	GE Healthcare	Iohexol	140, 180, 210, 240, 300, 350	Low-osmolar, nonionic
Ultravist	Bayer	Iopromide	150, 240, 300, 370	Low-osmolar, nonionic
Optiray	Covidien	Ioversol	240, 300, 320, 350	Low-osmolar, nonionic

There are many different types of contrast medium, and although they are similar in their applications, their core properties vary from manufacturer to manufacturer. Table 12.1 shows some of the most common CT contrast media in use today along with various specifications. It is important to note that not all of these contrast media are suitable for intrathecal use.

12.1.2 Pharmacology and Good Practice in Contrast Administration

As previously stated, all intravenous contrast media are iodine derivatives, and when injected intravenously, they have various effects on the body. Consequently, an understanding of the various properties is essential to ensure the clinical professional can make informed decisions and take actions to minimize risks to patients.

Due to the variations in the active substances used, it is advised that manufacturer's product information sheets are reviewed prior to administration. Absolute contraindications, as given by the manufacturers, could include hypersensitivity to the active substance, in this case iodine, or any of the excipients of the solution. If a patient has previously sustained a severe contrast reaction, then this may result in that contrast media not using in a future examination or an alternative examination being performed. There are other special precautions necessary with the use of contrast agents that are not absolute contraindications but put the patient at higher risk of adverse reaction. These would include a positive history of multiple well-documented allergies such as asthma and conditions associated with renal impairment [6].

Another consideration is for patients who are receiving metformin therapy. Metformin is a drug used primarily in diabetic patients but often in the treatment of polycystic ovaries. As metformin is solely excreted by the kidneys, any reduction in renal function, for example, following the introduction of a contrast medium, can result in reduced excretion; in turn this can lead to a condition known as lactic acidosis. The procedure used to manage patients on metformin therapy varies from department to department. The Royal College of Radiologists (RCR) has published guidance [6] which suggests that unless a patient's renal function is outside of their normal reference range, metformin therapy need not stop. As a precaution, many X-ray departments have ceased metformin therapy for 48 h post contrast injection.

This is in line with advice contained within the British National Formulary [8]. Some continue with this practice and even ask that a normal renal function test is obtained prior to recommencing metformin treatment.

Contrast administration to pregnant patients should occur only in exceptional circumstances as there is a small risk of thyroid suppression in the fetus [6]. X-ray imaging may also be undesirable due to the radiation burden to the fetus. The risk of proceeding would need to be assessed against the relative benefits of the examination. This decision is generally taken following discussion between the referring clinician and the consultant radiologist. Current RCR guidance for breast-feeding is that no special precautions need to be taken.

As iodinated contrast agents can lead to serious reactions (anaphylactic and anaphylactoid), it is good practice to have emergency drugs and resuscitation equipment easily accessible. Patients should be observed for at least 15 min post injection, as this is when the majority of severe reactions occur. They should also remain in the department for 30 min post procedure to ensure that symptoms do not develop.

Present-day nonionic, low osmolar contrast agents are up to ten times safer than those previously used [6]. As a result, the likelihood of a major life-threatening contrast reaction is very small. Published incidence of severe reactions with nonionic agents is 0.04 % and very serious reactions is 0.004 % [6].

The practitioner performing the examination generally undertakes the delivery of the contrast medium following strict, departmental protocols. The overall responsibility, as with any delegation, lies with the medical practitioner who has prescribed it. Within the UK, the administration of contrast is often conducted by radiographers under a Patient Group Direction (PGD). This is a written instruction which complies with regulation and local quality standards. In the Royal College of Nursing document entitled, "Patient Group Directions – Guidance and Information for Nurses," [7] a PGD is described as an instruction relating to a prescription-only medicine (POM) which provides guidance as to the correct method of administration for an appropriately trained health-care professional (HCP). PGDs are utilized following formal sign-off by the delegating physician and agreed by a pharmacist. They allow designated health-care professionals to administer prescription-only medicines following an assessment of the patient without the requirement of a prescription produced by a medical practitioner or, other independent prescriber.

The management of the risk of complications following the administration of contrast medium is of paramount importance. Prescreening of the patient for the relative contraindications (see below) should reduce the possibility of complications arising. Other good practices include the use of the smallest dose possible to achieve the best quality diagnostic image, the use of premedication and the cessation of nephrotoxic drugs for the 24 h preceding the contrast examination. The use of low osmolar contrast medium in the lowest dose possible while maintaining patient hydration before and after the examination will all assist in the management of the risk of reaction to the contrast medium [9]. Simple steps such as the preheating of contrast medium before administration can assist in the reduction in the number of reactions as this process reduces viscosity [10].

Preexamination checks will highlight the patients at greater risk of allergic reaction to contrast medium and subsequently reduce the risk of an adverse event. All patients who are to receive contrast medium should be checked for:

- Previous contrast medium reactions
- Asthma
- Renal impairment
- Diabetes mellitus
- Metformin therapy

In most cases, the above information can be checked directly with the patient. A positive response to any of the above questions will not necessarily lead to a cancellation of the procedure. Instead, this will allow the prescribing medical practitioner to make an informed decision about the relative risks of administration against the risk of an adverse event. Generally, the final decision to proceed with administration would lie with the radiologist supervising the examination.

The team within radiology should consist of professionals who are skilled in identification of symptoms of contrast medium reaction and trained medical practitioners who are able to competently deal with severe contrast media reactions. This is often the crash team contacted via a local emergency phone number; however, it is essential that the facilities and consumables required for management of adverse reactions are readily available within the department for immediate use.

Any adverse reactions should be accurately recorded within the body of the radiological report to provide a permanent record for future examinations. This will aid future decision making with regard to the techniques used, alternative imaging modalities or premedication. It is worth noting that the value of premedication to minimize the risk of severe contrast medium reaction is questionable [11]. A systematic review completed by Tramer et al. demonstrated a lack of evidence to suggest that routine premedication would assist in the prevention of severe allergic reactions.

Contrast-induced nephropathy (CIN) can also occur as a result of the administration of contrast medium. CIN can be defined as the decline in renal function within 72 h of the administration of contrast medium without any other known cause. This can result in acute renal failure which is clearly very important clinically and can be very costly due to potential for extended length of stay and/or additional requirement for treatment. There are various strategies that can be used in an attempt to manage the risk, and this primarily centers around the identification of the high-risk patients. The incidence of CIN with LOCM in the general population is <2 %; however, in high-risk groups, that is, diabetics or patients with renal impairment, the incidence of CIN is thought to be between 12 and 50 %. Published mortality rates with CIN suggest that if CIN occurs, 16 % of patients will die within 30 days and 25 % within 12 months. If CIN does not occur, the mortality rate is 3.2 % within 30 days and 1.2 % within 12 months. Prescreening of patients undergoing contrast medium injections should occur to minimize the risk. Identification of the high-risk patients and acting accordingly should help to reduce the incidence of CIN. An audit undertaken at a Manchester (UK) teaching hospital identified that of 100 CT

request cards scrutinized, none of the requests included the renal function of the patient. Subsequent analysis showed that 64.5 % of these patients had abnormal renal function (eGFR < 89 ml/min) at the time of imaging. Screening of patients for risk factors is essential; patients with renal impairment, diabetes, hypertension, and gout or those taking nonsteroidal anti-inflammatory (NSAIDs) drugs or diuretics are at higher risk.

12.1.3 The Management of Adverse Reactions

While the steps identified above will minimize the risks of using contrast media, adverse events will inevitably still occur. Subsequently, advice must be readily available for patient management following a reaction.

Possibly the most common reaction is nausea and/or vomiting which is generally managed by providing support, but in prolonged cases of vomiting, antiemetic medication should be considered. Other reactions are rare and include:

- Urticaria
- Bronchospasm
- Laryngeal edema
- Hypotension
- Anaphylactoid reaction

Management of the above ranges from antihistamine administration through intramuscular adrenaline to summoning the crash team.

Psychological preparation of the patient is an essential part of any examination, and patients warrant an explanation of the examination to be performed. As well as improving patient compliance, a thorough explanation of the procedure enables the patient to give the necessary informed consent.

All contrast reactions, regardless of severity, need to be clearly documented so that this information is readily available should the patient attend for a further contrast examination. The information is usually stored on the patient's electronic records/case notes. The patient should also be advised, if they have had a reaction to contrast, that they should make imaging staff aware of this information at any future X-ray appointments which may require the administration of contrast media.

12.1.4 The Role of Contrast Medium in CT Scanning

In 1973, Sir Godfrey Hounsfield described the invention of CT scanning in the *British Journal of Radiology*. The development of this technology over the subsequent 37 years has made computed tomography an essential diagnostic tool in the assessment of a wide range of pathologies and conditions.

Table 12.2 The approximate Hounsfield units for various tissues and substances within the human body

Substance/tissue	HU
Air	−1,000
Fat	−50 to −100
Water	0
CSF	+15
Muscle	+40
Liver	+40 to 60
Contrast	+130
Bone	+400

The physics of CT scanning is complex and as such will not be discussed in depth within this chapter. Instead, the chapter aims to discuss the basics of image formation with subsequent reference to the reasons for contrast medium usage.

Intravenous contrast medium is widely used within CT. Approximately 80 % of CT examinations involve the use of IV contrast media; approximately 65 % of CT examinations use oral contrast medium.

Table 12.2 illustrates the approximate Hounsfield units (HU, CT numbers) for various tissues and substances within the human body as calculated in CT.

HU forms the basis for CT image reconstruction and is based upon the attenuation coefficient of individual 3D tissue voxels, which are converted into 2D pixels and displayed within the resultant image. The similar HU of tissue described in Table 12.2 necessitates the use of contrast medium to increase the contrast between two adjacent structures. As contrast medium is iodine based, it inherently has a high atomic number and as such will attenuate the X-radiation to a greater extent than tissue which does not contain the contrast medium.

12.2 Injector Systems

Previously, when CT scan times could be in the order of 20 min for a routine abdomen and pelvis examination, injection of CT contrast was performed by hand. With the advent of multislice CT which has much faster acquisition times, more accurate timing of the contrast injection is required in order that the contrast is maintained in a bolus ensuring optimum enhancement of the tissues being imaged. It is now routine for intravenous contrast to be administered using a high flow rate (between 2 and 6 ml/s) via a pressure injector. This necessitates a cannula of adequate gauge (preferably 18G but no less than 20G) to be sited, preferably within the antecubital fossa.

As well as the obvious complications with contrast medium, there is also a risk of extravasation of the contrast medium at the injection site. Typically, this occurs when poor injection technique or practice occurs but is also more prevalent in certain groups of patient, for example, pediatrics, elderly patients, and patient with underlying cardiovascular disease. The cannula used should be of adequate gauge for the flow rate intended and ideally inserted immediately prior to use. It should be flushed with saline beforehand to check patency ensuring free flow of contrast

medium will occur. The incidence of extravasation following contrast medium has been demonstrated to be at approximately 0.07 % [12]. Severe reactions are only seen when large amounts of contrast medium are injected. The incidence of this complication has increased following the development of CT pressure injectors. It is good practice to observe the injection site for the duration of the injection for signs of extravasation. The injection can then be stopped immediately following extravasation being identified. However, this is not always possible if the scan commences concurrently which would yield a radiation burden to the staff member involved. To combat this, many manufacturers have developed automatic extravasation detection systems for their pressure injectors which minimize human error and the need for a staff member to be present during the injection or scan phase. The severity of the contrast extravasation is proportional to the amount of contrast that has extravasated. Recent studies have shown that moderate to severe reactions are typically only observed when in excess of 50 ml is extravasated [12].

Signs of extravasation include tightening of the skin, pain, and development of swelling underneath the skin. If any of these are observed, it is recommended that the contrast injection is ceased and the injection site examined closely.

Manual hand injections are still used when imaging the brain with contrast agent as the procedure tends not to be dynamic. Contrast enhancement of the brain is optimal between 1 and 3 min following injection of the contrast medium; however, contrast-enhanced imaging of the brain has been successfully achieved up to 1 h following contrast administration [13]. Normal brain tissue will not enhance with contrast medium, but in the event of disruption to the blood/brain barrier, the abnormal tissue will enhance with associated difference in attenuation value of the tissue which will increase the contrast between this and the normal brain tissue. This allows for better characterization of lesions than compared with CT undertaken without contrast.

Hand-delivery techniques can also be used if the cannula gauge does not allow for pressure injector usage; the injection site is at high risk of extravasation or in other delayed examination – for example, CT urogram – when bolus optimization is of limited importance.

12.2.1 Delivery Techniques

Modern-day multislice CT requires accurate, consistent delivery of contrast medium to ensure the best diagnostic quality can be achieved. Vascular organs throughout the body are enhanced to varying degrees by the contrast medium injected. Scanning should occur in the correct vascular phase to demonstrate the organ or pathology which will answer the clinical question. Possibly the most common example of this is demonstration of the liver using the portal venous phase of circulation. Typically, CT imaging of the liver will occur 60–70 s following the commencement of the contrast medium injection. Scanning is performed in various phases when imaging the liver with CT including the arterial, portal venous, and others and appreciable

differences in attenuation values of the liver tissue can be seen. Often imaging of this type will be completed using 70–90 ml of contrast medium injected at a rate of 3/4 ml/s.

Another good example of a delivery technique in common use involves a dual-phase injection when imaging the tissues of the neck. Due to the complex anatomy, a common protocol for imaging of the soft tissues of the neck when investigating a soft tissue tumor is as follows: A dual-phase injection technique is often utilized. Generally, 90 ml is injected, 50 ml at a rate of 2 ml/s followed by the remaining 40 ml at 1 ml/s. The complete injection will be administered in around 65 s. A delay is then built into the protocol so that scanning commences at 85–90 s. This ensures contrast enhancement within:

- Venous circulation
- Arterial circulation
- Tumor blush

This technique allows better tissue characterization than previous methods which often included arterial circulation only.

The optimization of the bolus of contrast is essential to ensure enhanced diagnostic images. The delivery techniques must attempt to minimize the volume of contrast injected while increasing the time period of enhancement.

The continuous development of MDCT has led to a corresponding decline in the use of diagnostic angiography. CT angiography is now widely accepted as a safe, effective, and sensitive alternative to conventional angiography. Conventional angiography still has a role within diagnostic radiology, but typically this is regarded as an interventional tool. A good example of the application of CT angiography is demonstrated in Fig. 12.3. The images demonstrate a basilar tip aneurysm on CT (Fig. 12.3a) and conventional, digital subtraction angiography (Fig. 12.3b). The CT imaging performed prior to the start of the embolization demonstrates the aneurysm neck and subsequently influences the decision on best course of treatment. Had the neck of the aneurysm been too wide, the patient would not have been fit for endovascular repair, and subsequently the aneurysm would have been clipped with invasive surgery. Figure 12.3c was produced using rotational angiography and offers essential information on planning the aneurysm repair.

Perfusion techniques are proving useful in the evaluation of acute stroke and in brain and liver lesions. The most promising area for development is the evaluation of the ischaemic penumbra which may provide accurate definition of the recoverable brain tissue with thrombolytic treatment. As with angiography, delivery of the contrast medium is required at a flow rate of 4/5 ml/s. A volume of approximately 50 ml will usually suffice. CT images are acquired over a period of approximately 1 min, commencing prior to the contrast delivery and ending following the flow of contrast through arterial, capillary, and venous circulation in the brain. The image dataset produced is subsequently processed to produce a series of maps which can provide visual analysis of the brain. Correlation with the conventional CT imaging allows an accurate diagnosis of acute stroke to be made.

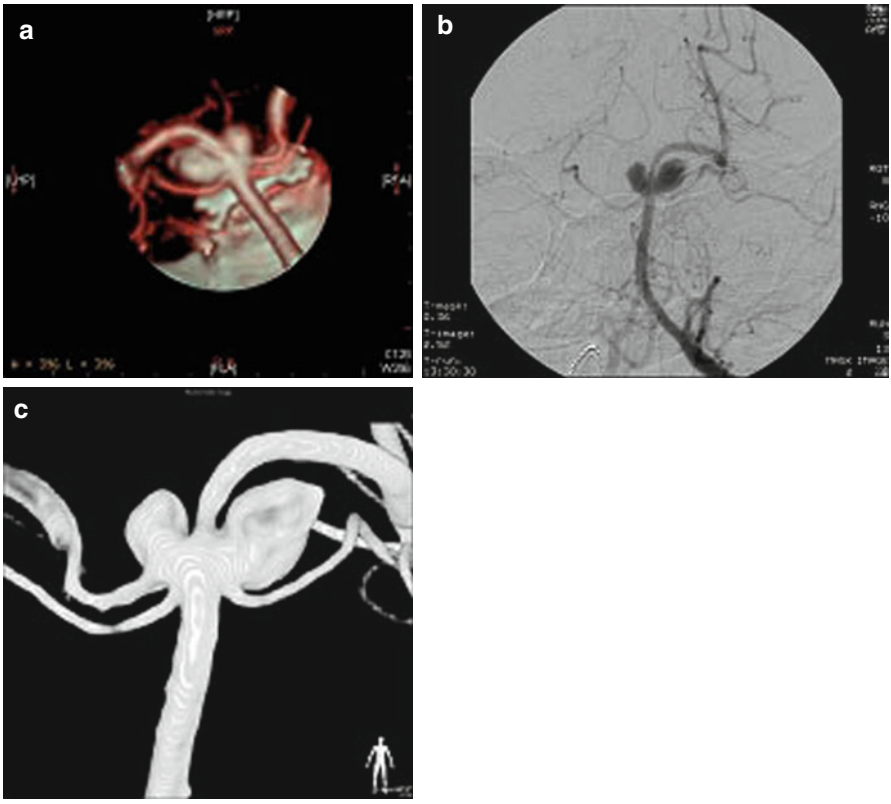

Fig. 12.3 (**a**) CT; (**b**) digital subtraction angiography; (**c**) rotational angiography

Most contrast media can be administered intrathecally; however, in other cases, this practice is contraindicated. This practice is most commonly used in CT myelography, but this technique generally only occurs in specialist neurosurgery centers and in cases where magnetic resonance imaging is contraindicated.

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