

**Review Article****Contrast Agents In computed tomography: A Review**

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## ABSTRACT

CT is a non-invasive diagnostic tool that allows for three dimensional visual reconstruction and slices of tissues of interest. CT imaging today is less time consuming, less expensive, and more readily available when it is compared with MRI and positron emission tomography (PET). The identification of a disease may be difficult due to very low contrast between pathological tissues for example tumors and metastases, organ structures and tissues around the site of interest. Contrast agents are boon in dentistry since it increases the density of tissues of desired area and thus blocks x-ray transmission thereby helps in better visualization of the structures. The choice of contrast agent depends on routes of administration, desired region of interest, suspected diagnosis and it should be non toxic to the tissues. This article is a review on contrast agents, their adverse effects and management.

**Introduction**

Contrast Enhanced Computed tomography studies of various body parts achieve increased attenuation in tissue of interest without intervention from surrounding structures. Multi detector contrast enhanced computed tomography replaces several conventional diagnostic imaging methods with faster examination, excellent contrast enhancement, perfusion measurement and multiplanar capabilities. **contrast agents** improves the visibility of internal bodily structures in imaging techniques such as computed tomography (CT). When an agent enhances visibility of a particular area, it is called "contrast enhancing".<sup>1</sup> When tissues of interest are less than 50 HU Contrast agents results in greater differences in CT attenuation and thereby improves the

quality of the images. Hence, contrast imaging agents are often used and required for better visibility of the tissue of interest by X-ray CT.<sup>1</sup>

**Ideal Requirements of contrast agents:**

- The contrast agent must improve the visualization of the area of interest by increasing the absolute CT attenuation difference between the target tissue and surrounding tissue and fluids;
- The imaging media should contain a high mol% of the X-ray attenuating atom per agent thereby reducing the volume and concentrations of contrast media needed for imaging;

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- The retention-time of the contrast agent in the tissues should be sufficiently long for completion of a CT scan ;
- The contrast agent must localize the tissue of interest and possess favorable biodistribution and pharmacokinetic profiles;
- The contrast agent should be readily soluble or form stable suspensions at aqueous physiological conditions with low viscosity;
- The contrast agent and its metabolites should be non-toxic; and
- The contrast agent should be cleared from the body in a reasonably short amount of time, usually within 24hrs.<sup>1</sup>

### Types of contrast agents

Iodine(Z=53) was first introduced as the atom of choice in imaging applications of computed tomography. First water-soluble imaging agents which were introduced are sodium and lithium iodide. Small-molecule iodinated contrast agents can be separated as “ionic,” and the “non-ionic” molecules. Ionic compounds interact with greater tendency to biological structures. Due to high osmolality of ionic contrast agents renal toxicity, vasodilatation, bradycardia, pulmonary hypertension occurs. Pain at the site of injection is more common with ionic contrast media. High-osmolality contrast media results in lower radio-density due to osmotic dilution.<sup>2</sup>

To overcome the problems associated with high-osmolality, non-ionic iodinated contrast media are used. These non-ionic contrast agents possess lower osmolality and lower adverse effects. All currently used ICM are chemical modifications of a 2,4,6-triiodinated benzene ring. Contrast agents are water soluble due to hydroxyl and amide groups. Ionic

contrast media are classified on the basis of their physical, chemical characteristics, chemical structure, osmolality, iodine content, and ionization in solution. Routinely in practice categorization based on osmolality is widely used.<sup>2</sup>

### High osmolality contrast media

Chemical structure of high osmolality contrast media consist of a tri-iodinated benzene ring with 2 organic side chains and a carboxyl group. The ionization at the carboxyl-cation bond makes the agent water soluble.<sup>3</sup> The osmolality in solution ranges from 600 to 2100 mOsm/kg, versus 290 mOsm/kg for human plasma. Adverse reactions of contrast media are usually based on osmolality.<sup>3</sup>

### Low osmolality contrast media:

There are 3 types of low-osmolality ICM:

(1) nonionic monomers, (2) ionic dimers, and (3) nonionic dimers.

### Nonionic monomers

The structure of non ionic monomers consist of tri-iodinated benzene ring, hydrophilic hydroxyl group. Because of the presence of hydrophilic group, it is made water soluble. Nonionic monomers do not ionize in solution due to lack of carboxyl group. Thus, for every 3 iodine atoms, only 1 particle is present in solution. Therefore, at a given iodine concentration, nonionic monomers have approximately one half the osmolality of ionic monomers in solution. At normally used concentrations, 25-76%, nonionic monomers have 290-860 mOsm/kg.<sup>3</sup>

Nonionic monomers are subclassified according to the number of milligrams of iodine in 1 mL of solution.

Name	Type	Iodine content	mOsm/kg	Osmolalitytype
<b>Ionic</b>				
<u>Diatriazoate(Hypaque 50)</u>	Monomer	300	1550	HOCM
<u>Metrizoate Isopaque(conray 370)</u>	Monomer	370	2100	HOCM
<u>Ioxaglate(Hexabrix)</u>	Dimer	320	580	LOCM
<b>Non Ionic</b>				
<u>Iopamidol(Isovue-370)</u>	Monomer	370	796	LOCM
<u>Iohexol(omnipaque 350)</u>	Monomer	350	884	LOCM
<u>Iodixanol(visipaque 320)</u>	Dimer	320	290	IOCM

Table 1:commonly used contrast media<sup>4</sup>

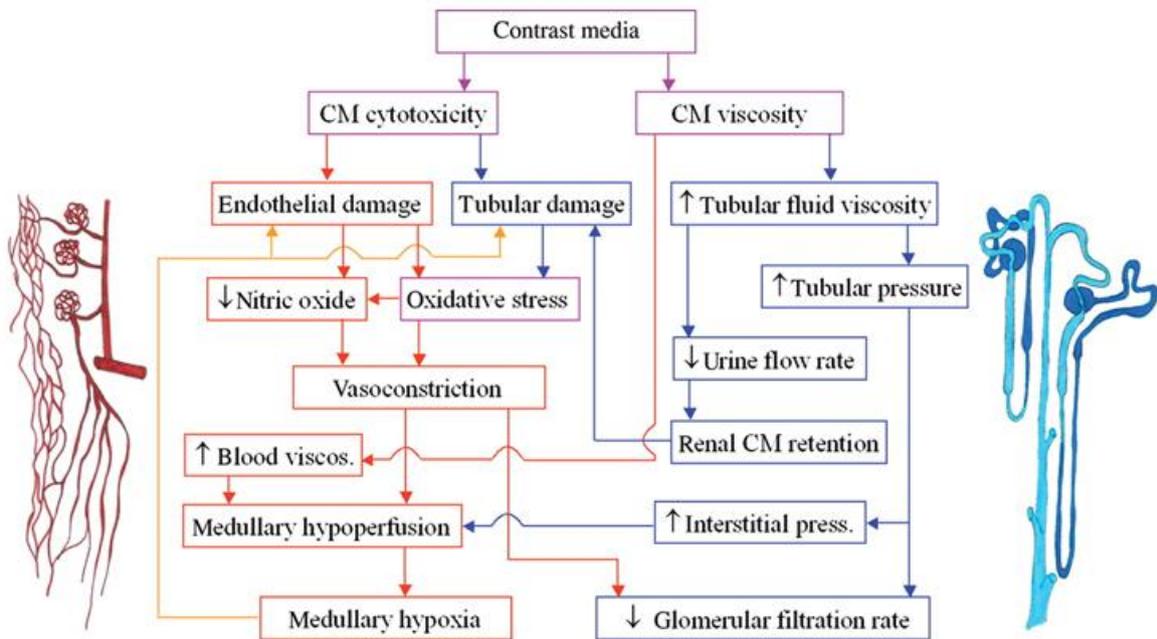


Fig:1 Pathogenesis of contrast media induced nephropathy<sup>7</sup>

Common nonionic monomers are iohexol , iopamidol , ioversol , and iopromide .<sup>3</sup>

The nonionic monomers are the contrast agents of choice. In addition to their non ionic nature and lower osmolalities, they are potentially less chemotoxic than the ionic monomers.<sup>3</sup>

### **Ionic dimmers**

The Ionic dimers are formed by joining 2 ionic monomers and eliminating 1 carboxyl group. It contain 6 iodine atoms for every 2 particles in solution . The only commercially available ionic dimer is ioxaglate . Ioxaglate has a concentration of 59%, or 320 mg I/mL, and an osmolality of 600 mOsm/kg. Due to high viscosity ioxaglate it is not manufactured in higher concentrations . Ioxaglate is used primarily for peripheral arteriography.<sup>3</sup>

### **Non ionic dimers**

Nonionic dimers are formed by joining two nonionic monomers. For every 1 particle there will be six iodine atoms in solution. The nonionic dimers have the lowest osmolality of all the contrast agents. At approximately 60% concentration by weight, these agents are iso-osmolar with plasma. Because of high viscosity they have limited clinical usefulness. Examples of nonionic dimers are iotrol and iodixanol .<sup>3</sup>

**Route of administration:** various studies on contrast media shows studies that intravenous contrast media has lesser side effects than intra-arterial contrast media . Radiographic contrast media are more nephrotoxic when given intra-arterially due to higher acute intrarenal concentration , particularly if the arterial injection is suprarenal. It has been shown that, while performing aortography, the closer the renal arteries

when injecting contrast medium , the higher the risk of CIN is.<sup>2</sup>

### **Factors Affecting Contrast Enhancement and Scan Timing**

Contrast enhancement at CT is affected by numerous interacting factors . These factors may be divided into three categories: patient, contrast medium, and CT scanning.

Since Iodine dose is commonly adjusted for body size on the basis of the 1:1 linear proportionality , it results in overestimation of the required iodine dose in obese patients. Iodine dose adjustment in obese patients should based on lean body weight or body surface.<sup>5</sup>

### **Cardiac Output and Cardiovascular Circulation**

The most important patient-related factor affecting the timing of contrast enhancement is cardiac output and cardiovascular circulation.

Women has lesser blood volume compared to males for a given body weight and height and this explains the clinical observation of higher contrast enhancement in female patients than male patients with the administration of a fixed iodine load per body weight<sup>5</sup>

### **Venous Access Site**

The arrival rate and Peak enhancement of contrast medium depends on the intravenous access sites. The preferred venous site is antecubital vein for intravenous contrast medium administration.

A fast injection is necessary for fast scan but requires more accurate scan timing. Faster injection rates with a fixed volume of contrast medium, the peaks of enhancement increase in magnitude earlier, but the duration of high magnitude enhancement decreases.<sup>5</sup>

Reaction	Etiology	Monitor	Treatment
<b>Anaphylactoid</b>			
urticaria	Anaphylactoid	Initial size with marking and follow	Usually none; diphenhydramine, 25–50 mg orally/intramuscularly/intravenously; epinephrine (1:1,000), 0.1–0.3 mL subcutaneously/intramuscularly
Bronchospasm	Anaphylactoid reaction	Oxygen saturation, pulse, BP	Secure airway; oxygen, 6–10 L/min; metaproterenol/terbutaline inhaler, 2–3 puffs; epinephrine (1:1,000), 0.1–0.3 mL subcutaneously/intramuscularly;
Facial or laryngeal edema	or Anaphylactoid reaction	Oxygen saturation, pulse, BP	Secure airway; oxygen, 6–10 L/min; call the emergency medical team if severe; epinephrine (1:1000), 0.1–0.3 mL subcutaneously/intramuscularly; epinephrine (1:10,000), 1 mL intravenously (slowly) if hypotensive; call the emergency medical team

Hypotension and tachycardia (fast pulse)	Vasodilation	Oxygen saturation, pulse, BP	Elevate legs 60°; oxygen, 6–10 L/min; rapid intravenous fluids; epinephrine (1:10,000), 1 mL intravenously (slowly); call the emergency medical team
<b>Nonanaphylactoid</b>			
Cardiac arrhythmia	Ionic abnormalities; chemical variations	Oxygen saturation, pulse, BP, ECG	Follow ACLS* protocols; call the emergency medical team
Hypertension	Histamine release of catecholamine	Oxygen saturation, pulse, BP, ECG	Nitroglycerine, 0.4 mg sublingually; nitroglycerine; 2% ointment; phenolamine, 5 mg intravenously for pheochromocytoma; call the emergency medical team
Seizures	Ionic abnormalities; chemOsmolar changes, causing large fluid volume shifts	Oxygen saturation, pulse, BP, ECG	Secure airway; oxygen, 6–10 L/min; diazepam, 5 mg intramuscularly/intravenously; midazolam, 0.5–1 mg intravenously; phenytoin infusion, 15–18 mg/kg at 50 mg/min; call the emergency medical team
Pulmonary edema	Osmolar changes, causing large fluid volume shifts	Oxygen saturation, pulse, BP, ECG	Secure airway; oxygen, 6–10 L/min; furosemide, 20–40 mg intravenously (slowly); morphine, 1–3 mg intravenously; call the emergency medical team

**Table 2:Management of contrast media reactions<sup>8</sup>**

**Injection duration**

**Contrast Medium Concentration**

- 1.To avoid injection at higher rate contrast medium is administered in high iodine concentration
2. A potential disadvantage of contrast medium with high concentration is high viscosity.<sup>5</sup>

Dose is considered a risk factor for adverse contrast reactions and nephropathy.The maximum recommended adult dose of iohexol (omnipaque;is of 250mL of omnipaque 350 or 291mL of omnipaque 300.<sup>6</sup>

### Contrast reactions

There are 2 basic types of contrast reactions; the first is the anaphylactoid reaction, and the second is the nonanaphylactoid reaction

Since Metformin is mainly eliminated via the kidneys (90%) it is advised in diabetic patients that metformin should be held 24-48 h before CM exposure to avoid the risk of lactic acidosis and restarted when clinically appropriate (e.g. no development of CIN or when renal function returns to baseline).<sup>9</sup>

### Conclusion

Iodinated CM stays as the sole agent for diagnostic and interventional vascular procedures. To prevent contrast media reactions always use minimal volume of contrast media and avoid administration of nephrotoxic medications with contrast agents as possible.<sup>10</sup>

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