MODERN RADIOLOGY eBook

Contrast Agents 对比剂

EUROPEAN SOCIETY OF RADIOLOGY

Preface

Modern Radiology is a free educational resource for radiology published online by the European Society of Radiology (ESR). The title of this second, rebranded version reflects the novel didactic concept of the ***ESR eBook*** with its unique blend of text, images, and schematics in the form of succinct pages, supplemented by clinical imaging cases, Q&A sections and hyperlinks allowing to switch quickly between the different sections of organ-based and more technical chapters, summaries and references.

Its chapters are based on the contributions of over 100 recognised European experts, referring to both general technical and organ-based clinical imaging topics. The new graphical look showing Asklepios with fashionable glasses, symbolises the combination of classical medical teaching with contemporary style education.

Although the initial version of the ***ESR eBook*** was created to provide basic knowledge for medical students and teachers of undergraduate courses, it has gradually expanded its scope to include more advanced knowledge for readers who wish to 'dig deeper'. As a result, *Modern Radiology* covers also topics of the postgraduate levels of the *European Training Curriculum for Radiology*, thus addressing postgraduate educational needs of residents. In addition, it reflects feedback from medical professionals worldwide who wish to update their knowledge in specific areas of medical imaging and who have already appreciated the depth and clarity of the ***ESR eBook*** across the basic and more advanced educational levels.

I would like to express my heartfelt thanks to all authors who contributed their time and expertise to this voluntary, non-profit endeavour as well as Carlo Catalano, Andrea Laghi and András Palkó, who had the initial idea to create an ***ESR eBook***, and - finally - to the ESR Office for their technical and administrative support.

Modern Radiology embodies a collaborative spirit and unwavering commitment to this fascinating medical discipline which is indispensable for modern patient care. I hope that this ***educational*** tool may encourage curiosity and critical thinking, contributing to the appreciation of the art and science of radiology across Europe and beyond.

Minerva Becker, Editor
Professor of Radiology, University of Geneva, Switzerland

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章节大纲：

前言

*《现代放射学》*是由欧洲放射学协会 (European Society of Radiology, ESR) 在线发布的免费放射学教育资源。第二版（更名版）标题反映了 ***ESR 电子书***新颖的教学概念，它以简洁页面的形式巧妙地融合文本、图像和示意图，并辅以临床影像学案例、问答部分和内容超链接，使读者能够在各基于器官的部分、更具技术性的章节、摘要以及参考文献之间快速切换浏览。

其章节以 100 多名公认欧洲专家的优秀稿件为根基，涉及各类一般技术和基于器官的临床影像学主题。同时采用了全新的图形外观，展示了佩戴时尚眼镜的 Asklepios，象征着传统医学教学与现代风格教育的结合。

虽然初版 ***ESR 电子书***旨在为医学生和本科生教师提供医学基础知识，但现已逐渐扩充其知识领域，为希望“深入挖掘”的读者提供了更多高阶技术知识。因此，*《现代放射学》*还涵盖了*欧洲放射学培训课程*研究生水平的各类主题，旨在解决住院医师的研究生教育需求。此外，书中还囊括了全球医疗专业人士的反馈，他们希望更新自己在医学影像特定领域的知识，并对 ***ESR 电子书***在基础和高等教育水平上的深度和清晰度表示高度赞赏。

我要衷心感谢所有为这项非营利活动自愿贡献时间和专业知识的作者，以及最初提出创作 ***ESR 电子书***的 Carlo Catalano、Andrea Laghi 和 András Palkó，最后还要感谢 ESR 办公室所提供的技术和行政支持。

*《现代放射学》*充分体现了医者的协作精神和对这门热门医学学科坚定不移的承诺，这是现代患者护理必须具备的优秀精神品质。我希望这款***教育***工具能够激励各位始终保持好奇心和批判性思维，从而促进整个欧洲乃至欧洲以外地区对放射学艺术和科学的认识。

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Thank you to Chinese radiology experts for bridging languages and open the world-class English resource by ESR to every Mandarin-speaking student, fueling global radiology talent with a single click

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翻译致谢

对比剂

章节大纲：

本章节为《现代放射学电子书》的部分译文。

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对比剂

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译者寄语：
感谢中国放射学专家们的倾力奉献！
你们跨越了语言的鸿沟，将欧洲放射学会 (ESR) 的世界级学术宝库呈献给广大中文学子。如今，前沿智慧一键即达，为全球放射学人才的蓬勃发展注入了强劲动力。

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MODERN RADIOLOGY eBook

Based on the ESR Curriculum for Radiological Education

Contrast Agents

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章节大纲：

基于 **ESR** 课程的放射学教育

对比剂

作者

Johannes Fröhlich | Gabriella Hänggi

所属机构

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章节大纲：

对比剂

/ Contrast Agents

Contrast agents are used to improve visualisation of an organ, tissue, or pathologic condition in diagnostic imaging by altering the attenuation of X-rays or by changing the response to the applied electromagnetic or ultrasound energy. They are substances used for diagnostic purposes only, without any pharmacodynamic activity, and are generally eliminated rapidly without metabolisation.

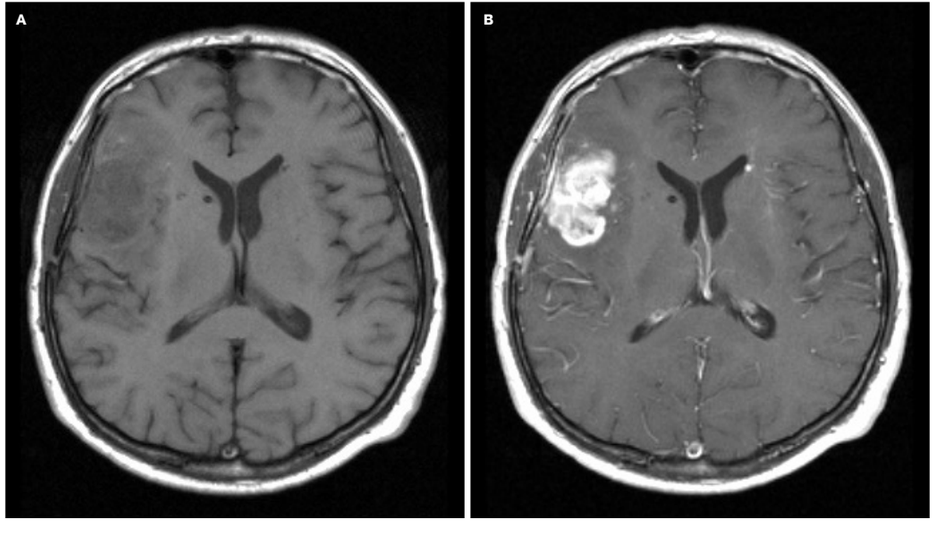

FIGURE 1

Brain MR-image pre-contrast (**A**) and after iv. administration of contrast (**B**).

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在诊断成像中，对比剂可改变 X 线的衰减程度，或改变对所施加的电磁能或超声能量的响应，从而改善器官、组织或病理状况的可视化。它们仅用于诊断目的，无任何药效学活性，通常消除迅速，且不会发生代谢。

图 1

静脉注射对比剂前 (**A**) 和静脉注射对比剂后 (**B**) 的脑部 MR 图像。

X-Ray Contrast Media (RCM)

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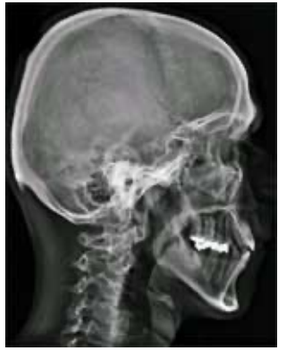
X 线对比剂 (RCM)

/ Classification

X-ray contrast media, also called **radiographic contrast media (RCM)**, enhance image contrast by locally inducing a change in X-ray absorptivity, which can be stronger (positive RCM) or weaker (negative RCM) than in the adjacent normal tissue.

Positive RCM

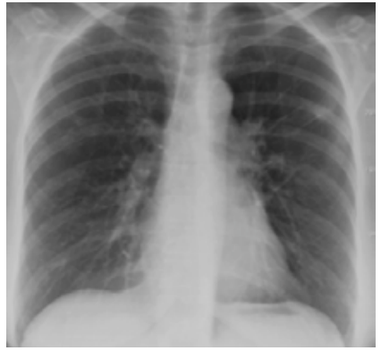


Substances with a high radiodensity, containing atoms with a high atomic number such as Barium ($^{56}Ba^{2+}$), Iodine ($^{53}I^{-}$) or gadolinium ($^{64}Gd^{3+}$) (off-label), lead to enhanced absorption of X-rays.

FIGURE 2

Positive contrast due to the bones.

Negative RCM



Substances with a low density, such as CO_2, Xe and air, lead to reduced absorption of X-rays.

FIGURE 3

Air in the lungs appears black because of less absorption of the X-rays: **negative** contrast.

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/ 分类

X 线对比剂，也称为**放射对比剂（radiographic contrast media，RCM）**，通过局部诱导 X 线吸收系数的变化来增强图像对比度，变化后的吸收系数可强于（阳性 RCM）或弱于（阴性 RCM）相邻正常组织的吸收系数。

阳性 RCM

含有高原子序数原子的高放射密度物质，如钡（$^{56}Ba^{2+}$）、碘（$^{53}I^{-}$）或钆（$^{64}Gd^{3+}$）（超说明书使用），会增强 X 线的吸收。

阴性 RCM

CO_2、氙气和空气等低密度物质会降低 X 线的吸收。

图 2

骨骼产生的**阳性**对比。

图 3

由于对 X 线的吸收较少，肺部的空气会呈现黑色：即**阴性**对比。

/ Iodinated RCM

Iodinated RCM are available as water soluble, hydrophilic RCM or as oily, lipophilic RCM.

Oily, Lipophilic Iodinated RCM

Lipiodol is an oily lipophilic iodinated RCM, which is made of poppy seed oil whose unsaturated fatty acids were substituted with iodine. It is used for visualisation of fine structures in:

- direct lymphography (imaging of the lymphatic system)
- transarterial chemoembolisation of hepatocellular carcinoma (**Fig. 4**)
- some countries for hysterosalpingography (to determine tubal patency)

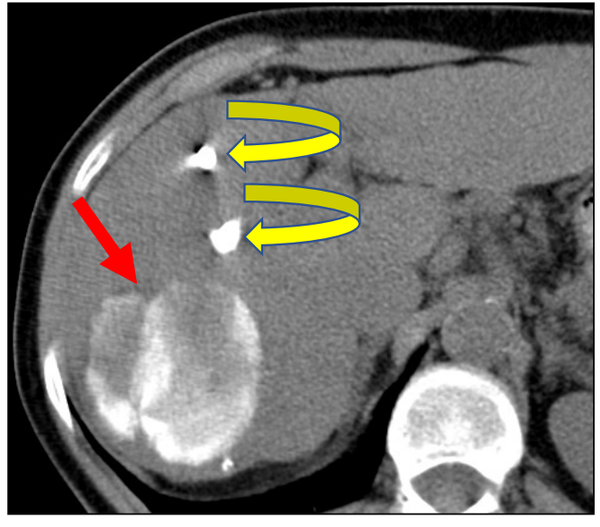

FIGURE 4

Control CT image obtained after transarterial chemoembolisation of a **hepatocellular carcinoma (HCC)** with Doxorubicine/Lipiodol and portal vein embolisation with Lipiodol/bucrylate (to induce left liver lobe hypertrophy). Residual Lipiodol in HCC (red arrow) and in the embolised portal branches (yellow arrows). Image courtesy: Christoph Becker, MD, University of Geneva.

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/ 碘化 RCM

碘化 RCM 分为水溶性亲水性 RCM 和油性亲脂性 RCM。

油性亲脂性碘化 RCM

碘油是一种油性亲脂性碘化 RCM，由罂粟籽油制成，其不饱和脂肪酸被碘取代。它用于以下精细结构的显影：

- 直接淋巴系统造影（淋巴系统成像）
- 肝细胞癌的经动脉化疗栓塞（**图 4**）
- 某些国家/地区用于子宫输卵管造影（判断输卵管通畅性）

图 4

肝细胞癌（hepatocellular carcinoma，HCC）经动脉化疗栓塞（多柔比星/碘油）及门静脉栓塞（碘油/异丁基-2-氰丙烯酸盐，诱导左肝叶肥大）后获得的对照 CT 图像。HCC 内残留的碘油（红色箭头）和栓塞的门静脉分支内残留的碘油（黄色箭头）。图片来源：日内瓦大学医学博士，Christoph Becker。

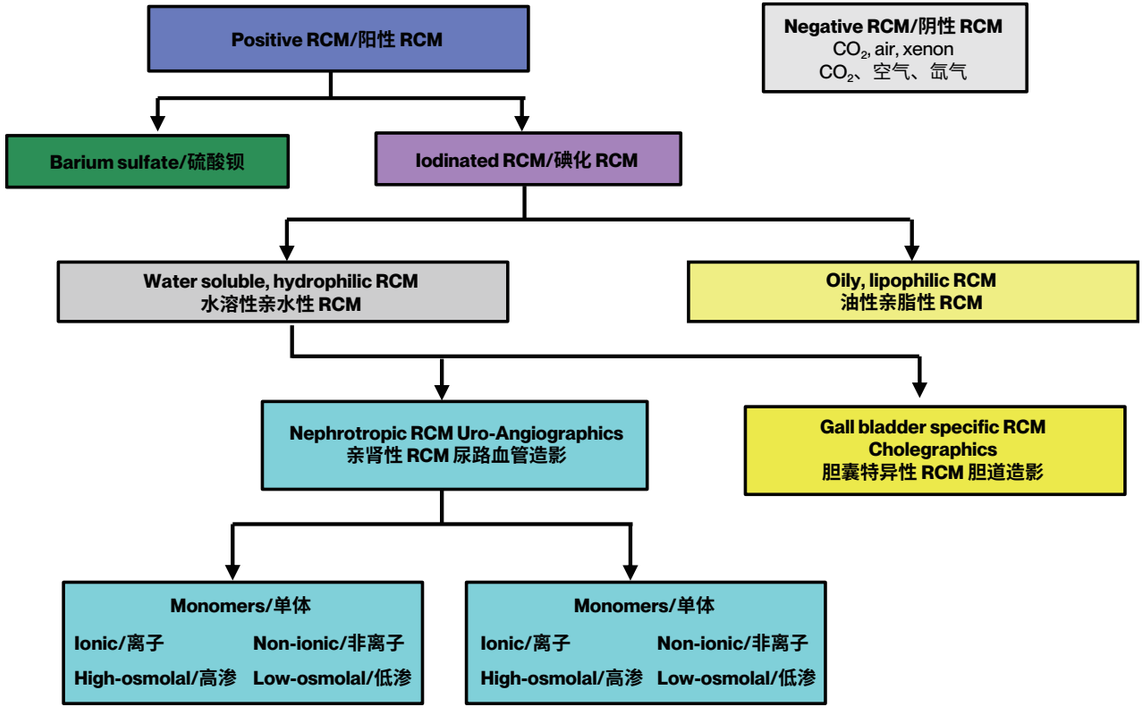

FIGURE 5

Classification of X-ray contrast media.

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图 5

X 线对比剂的分类。

Water Soluble, Hydrophilic Iodinated RCM

The water soluble, hydrophilic RCM comprise nephrotropic RCM, which are employed for uro-angiographics, and gallbladder specific RCM, which were used for intravenous cholangiography.

Structure of Water soluble, Iodinated RCM

The basic structure of water-soluble iodinated RCM is a benzene ring, which is symmetrically substituted with three covalently bound iodine atoms:

- the presence of three iodine atoms in one molecule provides a high X-ray absorptivity with correspondingly high contrast density
- the covalent binding ensures a strong chemical bond of iodine and thus reduces the risk of toxic effects from released free iodide
- the remaining three, non-iodinated carbons of the benzene ring are substituted with respective chemical side-groups R1, R2 and R3

FIGURE 6

Basic structure of iodinated RCM.

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水溶性亲水性碘化 RCM

水溶性亲水性 RCM 包括用于尿路血管造影的亲肾性 RCM，以及曾用于静脉胆管造影的胆囊特异性 RCM。

水溶性碘化 RCM 的结构

水溶性碘化 RCM 的基本结构是一个苯环，对称地被三个共价结合的碘原子取代：

- 一个分子中有三个碘原子，对 X 线的吸收系数较高，对比密度也相应较高
- 共价结合可确保碘的化学键牢固，从而降低游离碘释放产生毒性作用的风险
- 苯环上剩余的三个非碘化碳原子分别被化学侧基 R1、R2 和 R3 取代

图 6

碘化 RCM 的基本结构。

Classification of the Nephrotropic RCM

Two major chemical variations, namely, monomeric versus dimeric and ionic versus non-ionic, result in four classes of RCM (Fig. 7):

Ionic monomeric RCM: one triiodinated benzene ring with a carboxylate functional group (-COO-) in one of the substituent groups

Ionic dimeric RCM: two triiodinated benzene rings linked by an organic bridging group with at least one carboxylate functional group (-COO-) in one of the substituent groups (not marketed anymore)

Non-ionic monomeric RCM: one triiodinated benzene ring without -COO- functional group, e.g., having an amide (-CO-NH-R) group instead of the -COO- functional group

Non-ionic dimeric RCM: two triiodinated benzene rings without -COO- functional group, e.g., having an amide (-CO-NH-R) group instead of the -COO- functional group, linked by an organic bridging group

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亲肾性 RCM 的分类

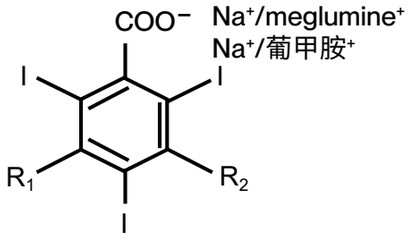
两种主要的化学差异，即单体与二聚体、离子型与非离子型，形成了四类 RCM（图 7）：

离子型单体 RCM：具有一个三碘化苯环，其中一个取代基含有羧酸官能团 (-COO-)

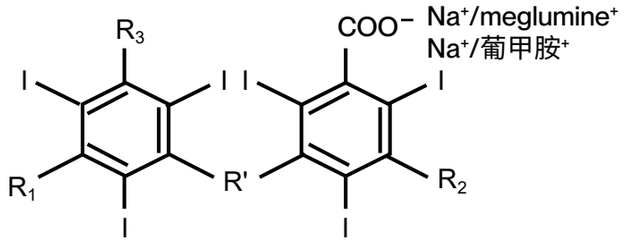
离子型二聚体 RCM：两个三碘化苯环通过一个有机桥接基团连接，其中一个取代基中至少含有一个羧酸官能团 (-COO-)（已不再销售）

非离子型单体 RCM：具有一个三碘化苯环，不含 -COO- 官能团，例如，以酰胺基 (-CO-NH-R) 取代 -COO- 官能团

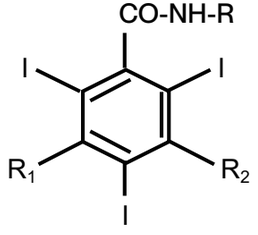
非离子型二聚体 RCM：两个不含 -COO- 官能团的三碘化苯环（例如，以酰胺基 [-CO-NH-R] 取代 -COO- 官能团）通过有机桥接基团连接而成



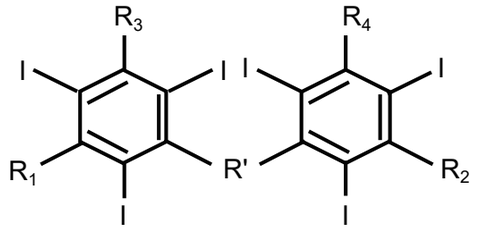
Ionic monomeric high osmolar RCA
离子型单体高渗 RCA



Ionic dimeric low osmolar RCA
离子型二聚体低渗 RCA



Non-ionic low osmolar monomeric RCA
非离子型低渗单体 RCA



Non-ionic isoosmotic dimeric RCA
非离子型等渗二聚体 RCA

FIGURE 7

Structure of the 4 classes of nephrotropic RCM.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

图 7

4 类亲肾性 RCM 的结构。

Ionic contrast agent – once dissolved, there's a dissociation into an anion and cation in the aqueous solution.

In the ionic RCM, the presence of a carboxylate group contributes to a net **negative** charge to the molecule, which is made available in neutral form, usually as a salt of sodium, calcium or methylglucamine cations.

The dissociation into negative and positive ions in ionic RCM ensures water solubility, while in **non-ionic** RCM any polar groups of the substituents R1, R2 and R3, particularly hydroxyl groups, are responsible for the water solubility.

The other substituents may further improve water solubility, influence the pharmacokinetics and safety properties, defining the elimination pathway, protein binding and/or tolerability.

Contrast Agents

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离子型对比剂 - 一旦溶解，在水溶液中会解离为阴离子和阳离子。

在离子型 RCM 中，羧酸酯基团的存在使分子带有净负电荷，该分子通常以中性形式存在，即钠、钙或甲基葡胺阳离子的盐类形式。

离子型 RCM 解离为阴离子和阳离子，从而确保其水溶性；而**非离子型** RCM 的水溶性则由取代基 R1、R2 和 R3 中的极性基团（尤其是羟基）决定。

其他取代基可进一步改善水溶性，影响药代动力学和安全性特性，决定消除途径、蛋白质结合和/或耐受性。

对比剂

章节大纲：

Gallbladder Specific RCM

An intravenous gallbladder specific RCM available as a salt of meglumine has a dimeric structure with two triiodinated benzene rings linked by an organic bridging group. This cholegraphic RCM comprises a carboxylate functional group at each benzene ring with no further side chains. The unsubstituted position in each benzene ring promotes plasma protein binding and a delayed glomerular filtration leading to excretion in the bile without chemically modifying the molecule.

However, the cholegraphic RCM have shown a higher incidence of adverse effects than the nephrotropic explaining the non-availability of these RCMs.

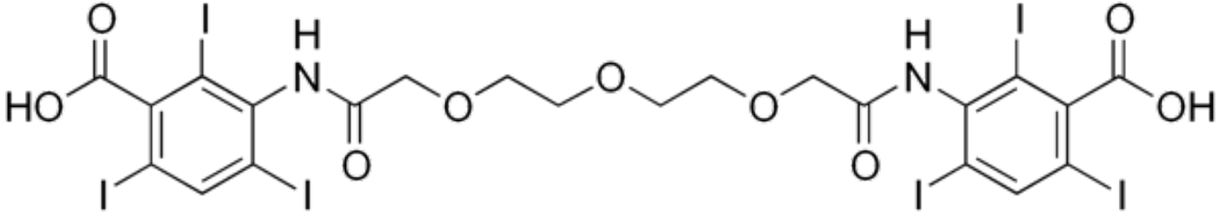

FIGURE 8

Structure of the gallbladder specific RCM.

Contrast Agents

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章节大纲：

胆囊特异性 RCM

以葡甲胺盐形式提供的静脉注射用胆囊特异性 RCM 具有二聚体结构，其中两个三碘化苯环通过一个有机桥联基团连接。这种胆道造影 RCM 在每个苯环上均包含一个羧酸官能团，且无其他侧链。每个苯环上的未取代位置可促进血浆蛋白结合，并延缓肾小球滤过，从而使对比剂无需经化学修饰即可通过胆汁排泄。

然而，与亲肾性 RCM 相比，胆道造影 RCM 已显示出更高的不良反应发生率，这也解释了为何这些 RCM 已不再可用。

图 8

胆囊特异性 RCM 的结构。

/ Physicochemical Properties of Iodinated RCM

The most important physicochemical properties of iodinated RCM which affect clinical practice are iodine concentration, osmolality, viscosity and hydrophilicity.

Iodine Concentration

The contrast enhancement is directly related to the local iodine concentration in the tissue.

Intravenous iodinated RCM are available in concentrations from **200 to 400 mg of iodine per millilitre** of the contrast solution, with a dosage of 300 mg/ml being clinically used in most cases.

The choice of the appropriate iodine concentration depends on the type of investigation, the disease and the diagnostic device used.

FIGURE 9

Example of a iodinated contrast agent: 300 mg/mL = 30% of iodine.

/ 碘化 RCM 的理化性质

影响临床实践的碘化 RCM 的最重要理化性质是碘浓度、渗透压、黏度和亲水性。

碘浓度

对比增强效果与组织中的局部碘浓度直接相关。

静脉注射碘化 RCM 的溶液浓度为**每毫升对比剂含 200 至 400 mg 碘**，临床最常用的浓度为 300 mg/mL。

应根据检查类型、疾病和所使用的诊断设备，选择适当的碘浓度。

图 9

碘化对比剂示例：300 mg/mL = 30% 的碘。

Osmolality

Osmolality is a measure of the number of dissolved active particles per kilogram of solvent, i.e., water, expressed in mOsm/kg H_2O at 20°C.

The osmolality of blood is 300 mOsm/kg H_2O, and the osmolality of the pain threshold is 600 mOsm/kg H_2O.

For a given iodinated RCM, osmolality increases linearly with iodine concentration.

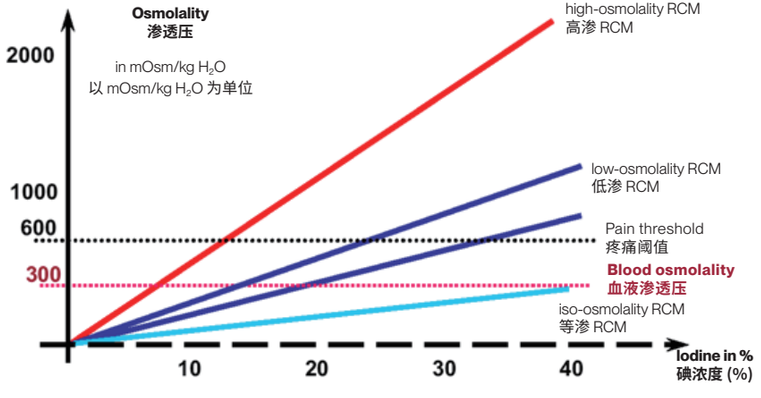

FIGURE 10

Osmolality as function of the iodine concentration. Osmolality, e.g., influences the pain sensation of the patient.

>=< FURTHER KNOWLEDGE

High-osmolality agents include ionic monomers, which for every 3 iodine atoms generate 2 solute particles; with the resultant osmolality being 5-8 times that of blood.

Low-osmolality agents include ionic dimers and non-ionic monomers, which for every 3 iodine atoms generate 1 solute particle; with the resultant osmolality being 1-3 times that of blood.

Iso-osmolal agents include non-ionic dimers, which for every 6 iodine atoms generate 1 solute particle; with the resultant osmolality being approximately equal to that of blood.

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章节大纲：

渗透压

渗透压是衡量每千克溶剂（即水）中溶解的活性颗粒数量的指标，在 20°C下以 mOsm/kg H_2O 表示。

血液的渗透压为 300 mOsm/kg H_2O，疼痛阈值的渗透压为 600 mOsm/kg H_2O。

对于给定的碘化 RCM，渗透压随碘浓度呈线性增加。

>=< 进阶知识

高渗性对比剂包括离子型单体，其每 3 个碘原子会产生 2 个溶质颗粒，最终渗透压为血液的 5～8 倍。

低渗性对比剂包括离子型二聚体和非离子型单体，其每 3 个碘原子产生 1 个溶质颗粒，最终渗透压为血液的 1～3 倍。

等渗性对比剂包括非离子型二聚体，其每 6 个碘原子产生 1 个溶质颗粒，最终渗透压与血液大致相等。

图 10

渗透压与碘浓度存在函数关系。例如，渗透压会影响患者的痛觉。

<!> ATTENTION

STRUCTURE	OSMOLALITY	VISCOSITY
High-osmolality ionic momomeres	1500 - 2100 mOsm/kg H_2O	+
Low-osmolality non-ionic monomers	500 - 900 mOsm/kg H_2O	++
Low-osmolality ionic dimers	600 mOsm/kg H_2O	+
Iso-osmolal non-ionic dimers	300 mOsm/kg H_2O	+++

TABLE 1

Osmolality and viscosity of iodinated contrast media.

Administration of a RCM with a high osmolality stimulates an inflow of water from the interstitial spaces into the vascular compartment, leading to hypervolaemia, vasodilatation, an increased cardio-vascular charge, bradycardia, a reflectoric drop in blood pressure, pulmonary hypertension and possibly endothelial damage.

Adverse effects attributable to high osmolality include vascular pain, flushing, discomfort, nausea, vomiting and an increase of diuresis and dehydration.

Contrast Agents

对比剂

CHAPTER OUTLINE:

章节大纲：

<!> 注意

结构	渗透压	黏度
高渗性离子单体	1500～2100 mOsm/kg H_2O	+
低渗性非离子单体	500～900 mOsm/kg H_2O	++
低渗性离子二聚体	600 mOsm/kg H_2O	+
等渗性非离子二聚体	300 mOsm/kg H_2O	+++

表 1

碘化对比剂的渗透压和黏度。

使用高渗透压的 RCM 会促使水分从组织间隙流入血管腔，导致血容量过多、血管扩张、心血管负荷增加、心动过缓、反射性血压下降、肺动脉高压，并可能造成内皮损伤。

高渗透压引起的不良反应包括血管性疼痛、潮红、不适、恶心、呕吐以及尿量增加和脱水。

Viscosity

Viscosity describes the flow properties of the contrast agent solution and is expressed in mPa.s.

Viscosity increases disproportionately with iodine concentration and it decreases significantly with increasing temperature.

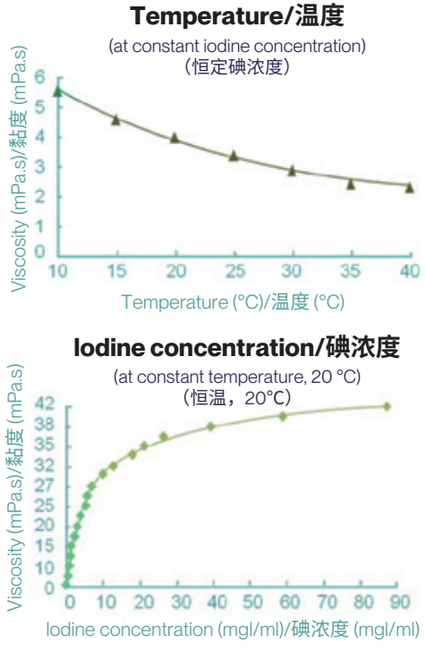

FIGURE 11

Viscosity in relation to the temperature and iodine concentration.

<!> ATTENTION

The viscosity of a contrast medium has an impact on the **maximum possible injection rate** and on the mixing behavior in the blood vessels.

Warming contrast medium to a temperature of 37°C reduces its viscosity and increases the efficiency of delivering high-viscosity agents in case of fast injection and/or passage through tiny catheters.

Viscosity plays an important role in **renal tolerance** of RCM, with near-serum viscosity reducing the risk of contrast-induced nephrotoxicity associated with iodinated RCM.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

黏度

黏度描述了对比剂溶液的流动性，以 mPa.s 表示。

黏度随碘浓度的增加呈非比例性升高，并随温度升高而显著降低。

<!> 注意

对比剂的黏度会影响最大可行注射速率及在血管中的混合行为。

将对比剂加热至 37°C 可降低其黏度，在快速注射和/或通过细小导管的情况下，可提高输送高黏度对比剂的效率。

黏度在 RCM 的肾脏耐受性中起重要作用，接近血清黏度可降低碘化 RCM 相关的对比剂诱发肾毒性风险。

图 11

黏度与温度和碘浓度的关系。

Hydrophilicity

Hydrophilicity refers to an affinity for water, e.g., to the tendency of a substance to **dissolve in water**, and can be expressed as log P (octanol-water distribution coefficient).

In iodinated RCM, the hydrophilicity depends on the **number of hydrophilic groups** such as OH and N groups that are present in the substituent chains of the inherently hydrophobic triiodobenzene core.

The **increased water solubility** of highly hydrophilic RCM reduces the binding to plasma proteins, thereby slowing down intracellular distribution of the RCM, accelerating renal elimination and reducing the passage through the blood-brain barrier. Accordingly, a high hydrophilicity **reduces** neurotoxicity, immunogenicity and nephrotoxicity and lowers the risk of allergic reactions.

Contrast Agents

CHAPTER OUTLINE:

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章节大纲：

亲水性

亲水性是指对水的亲和力，例如，物质**溶于水**的倾向，可用 log P（辛醇-水分配系数）表示。

在碘化 RCM 中，亲水性取决于**亲水基团的数量**，例如存在于固有疏水性三碘苯核心的取代基链中的 OH 和 N 基团数量。

高亲水性 RCM 的**水溶性增强**，可减少其与血浆蛋白的结合，从而减缓 RCM 的细胞内分布、加速肾脏排泄，并减少其通过血脑屏障的量。因此，高亲水性可**降低**神经毒性、免疫原性和肾毒性，并降低过敏反应的风险。

/ Pharmacokinetics of Iodinated RCM

Two-Compartment Model

The pharmacokinetics of iodinated RCM are best described using a two-compartment model:

Following **intravascular administration**, the iodinated RCM is rapidly distributed throughout the intravascular space, reaching a **peak plasma concentration** within 2 minutes, followed by a **passage into the interstitial liquid**, which is accessible through pores in the capillary walls.

The iodinated RCM thus introduced into the extracellular space cannot pass an intact blood brain barrier and is not distributed in the cellular compartment. However, it can cross the placental barrier in small amounts and is excreted in very small amounts in breast milk.

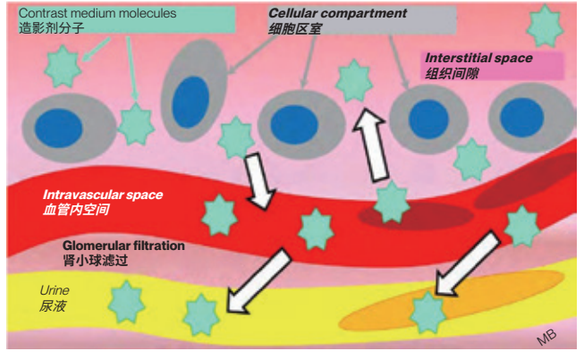

FIGURE 12

Two-compartment model with renal elimination.

Elimination of iodinated RCM occurs almost exclusively by **passive glomerular filtration**. With normal kidney function, the elimination half-life is approximately 90 minutes, and almost the entire applied dose is excreted within 24 hours. In case of renal impairment, the elimination half-life is considerably prolonged.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 碘化 RCM 的药代动力学

二室模型

碘化 RCM 的药代动力学最适合用二室模型来描述：

血管内施用后，碘化 RCM 快速分布至整个血管内空间，在 2 分钟内达到**血浆峰浓度**，随后通过毛细血管壁上的孔隙**进入组织间液**。

由此引入细胞外空间的碘化 RCM 不能通过完整的血脑屏障，并且不会分布在细胞区室中。但它可少量穿过胎盘屏障，也有极少量经母乳排出。

碘化 RCM 的消除几乎完全通过**肾小球被动滤过**实现。肾功能正常者的消除半衰期约为 90 分钟，且几乎全部施用剂量都会在 24 小时内排出体外。在肾功能损害的情况下，消除半衰期会显著延长。

图 12

肾消除二室模型。

Pharmacokinetics and Imaging

With regard to imaging with iodinated RCM, there are three post-injection phases:

- vascular phase, which is of very short duration of less than 1 minute, for imaging of arteries
- interstitial phase, which is of short duration of 1.5-10 minutes, for imaging of organs
- elimination phase, which is delayed post injection (5 minutes) but then of longer duration up to 30 minutes, for imaging of the urinary tract

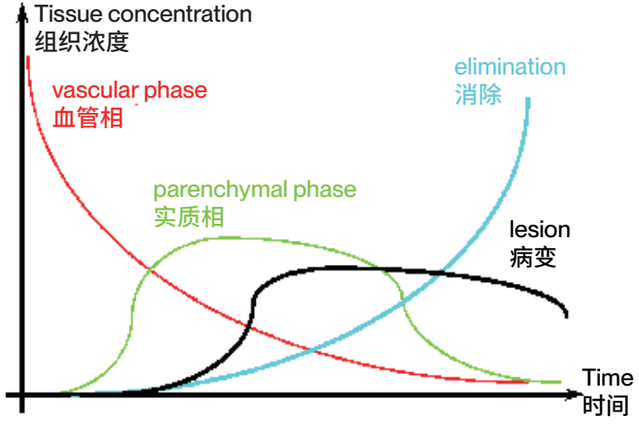

FIGURE 13

Post injection phase with iodinated RCM. Note the temporal contrast differences between the various spaces.

<!> ATTENTION

In general, the distribution from the intravascular compartment to **highly perfused organs**, such as brain, liver, and kidney, is **rapid**, whereas distribution to **less perfused organs** and tissues, such as bone and fat, is much **slower**.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

药代动力学和影像学

碘化 RCM 成像有三个注射后时相：

- 血管相，持续时间极短（不到 1 分钟），用于动脉成像
- 间质相，持续时间短，1.5～10 分钟，用于器官成像
- 消除相，注射后延迟出现（5 分钟），但持续时间较长，可达 30 分钟，用于泌尿道成像

<!> 注意

一般而言，从血管内腔室向高灌注器官（如脑、肝和肾）的分布迅速，而向低灌注器官和组织（如骨骼和脂肪）的分布则慢得多。

图 13

碘化 RCM 的注射后时相。注意不同空间之间的时间对比差异。

Opacification Modes of RCM

RCM are extensively used to visualise certain structures in the organism and to obtain information on organ function, which is achieved by applying four different modes of opacification:

Direct Luminal Filling

The identification of morphological structures is the main objective of direct luminal filling, which can occur through a natural access (**Fig. 14**) or through an iatrogenically created access. This mode of opacification permits the differentiation of superficial or mural changes, and it can provide functional information, e.g., about changes in tone or peristalsis in hollow passages.

Functional Organ Imaging

Functional opacification, which is applied in urography (**Fig. 15**) and cholegraphy, exploits the fact that the contrast density depends significantly on the functionality of the kidneys and urinary tract or the hepatobiliary system. Consequently, the radiographic assessment of these organs reveals both morphological and functional changes.

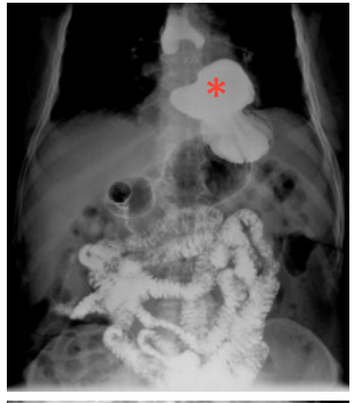

FIGURE 14

Barium X-ray (upper gastrointestinal tract) in a patient with hiatal hernia (asterisk). Note normal opacification of small bowel loops. Courtesy: Georgy Varnay, MD, University Hospitals Geneva.

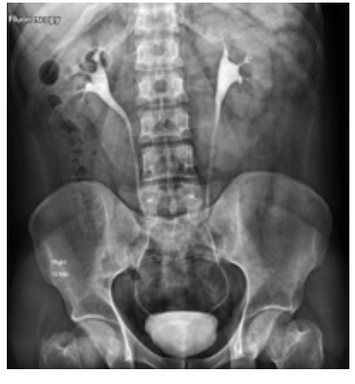

FIGURE 15

Normal urography. Case courtesy of Dr. MT. Niknejad, Radiopedia.org, rID: 85286.

Contrast Agents

CHAPTER OUTLINE:

RCM 的显影模式

RCM 广泛用于显示机体的特定结构并获取器官功能信息，可通过应用四种不同的显影模式来实现：

管腔内直接充盈

管腔内直接充盈的主要目的是识别形态结构，可通过自然通道(**图 14**）或医源性创建的通道实现。这种显影模式可用于区分表面或腔壁的病变，并且能够提供功能信息，例如关于中空管道的张力或蠕动变化的信息。

器官功能成像

功能性显影适用于尿路造影（**图 15**）和胆道造影，其利用的原理是对比剂密度在很大程度上取决于肾脏和泌尿道或肝胆系统的功能。因此，对这些器官的放射学评估可揭示形态学和功能性改变。

图 14

一名食管裂孔疝（星号）患者的钡餐 X 线检查（上消化道）。注意小肠袢显影正常。来源：日内瓦大学医院医学博士，Georgy Varnay。

图 15

正常尿路造影。病例来源：MT.Niknejad 博士，Radiopedia.org，rID：85286。

Parenchymal Enhancement

In parenchymal staining, enhancement of contrasts between tissues results from the passage and selective accumulation of RCM in different organs or tissues, thereby improving the differentiation of morphological structures, especially between normal and pathological tissues. This allows, or at least facilitates, the demonstration of pathological processes and of their etiology as well (**Fig. 16**).

Angiography

In angiography (**Fig. 17**), selective opacification can be achieved by direct RCM injection into the vessel of interest, followed by evaluation of RCM distribution and filling patterns including gaps in opacification of the target anatomy. This evaluation yields detailed diagnostic information regarding normal and abnormal morphology and function.

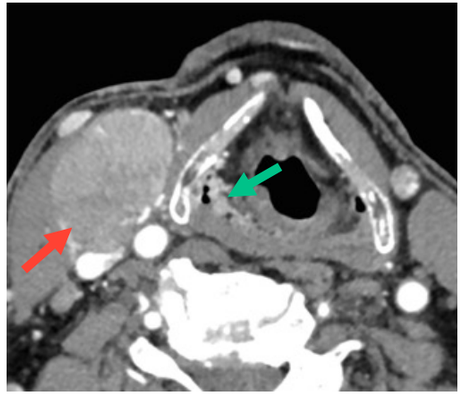

FIGURE 16

Contrast enhanced CT (parenchymal staining) showing a small tumour arising from the hypopharynx (green arrow) and a right lymph node metastasis (red arrow). Case courtesy: Minerva Becker, MD, University Hospitals Geneva.

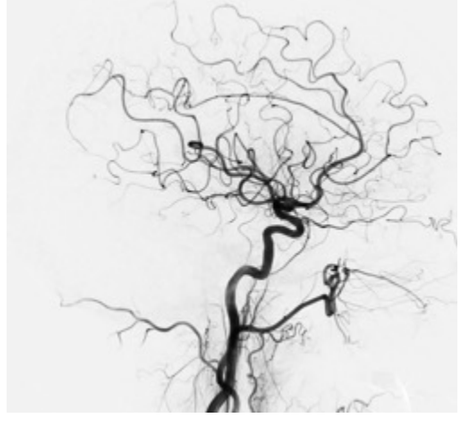

FIGURE 17

Normal angiography of the carotid arteries. Lateral view.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

实质强化

在实质显影中，由于 RCM 在不同器官或组织中的通过和选择性蓄积，组织之间的对比度会增强，从而改善了形态结构的区分，尤其是在正常组织与病理组织之间。这样就可以或至少有助于证明病理过程及其病因（图 16）。

血管造影

在血管造影术（图 17）中，通过将 RCM 直接注射到目标血管内可实现选择性显影，随后评估 RCM 的分布和充盈模式，包括目标解剖结构显影中的充盈缺损。该评估可提供关于正常和异常形态及功能的详细诊断信息。

图 16

对比增强 CT（实质染色）显示起源于下咽的小肿瘤（绿色箭头）和右侧淋巴结转移（红色箭头）。病例提供：日内瓦大学医院医学博士，Minerva Becker。

图 17

颈动脉的正常血管造影。侧视图。

/ Indications of RCM Application

Intravenous RCM Injection

Intravenous RCM administration for the purpose of CT scanning is **the most common use** of iodinated RCM and has a wide variety of indications. Intravenous administration first leads to an arterial opacification, which is followed by a parenchymal contrast enhancement.

For arterial opacification, the **rate of iodine delivery** plays a key role.

For the evaluation of a solid organ, such as the liver or pancreas, parenchymal organ enhancement depends primarily on the **total amount of iodine** administered, because lesion conspicuity may require a larger volume of contrast medium to be injected.

Applications of intravenous RCM administration:

- Computed tomography
- Digital subtraction angiography
- Intravenous urography
- Venography (phlebography)
  - Inferior vena cava and its tributaries
  - Superior vena cava and its tributaries
  - Extremities
- Other venous sites
  - Epidural venography

/ Contrast Agents

CHAPTER OUTLINE:

/ 应用 RCM 的适应证

/ 对比剂

章节大纲：

静脉注射 RCM

为进行 CT 扫描而静脉注射 RCM 是碘化放射对比剂的**最常见用途**，其适应证广泛。静脉注射后，首先会出现动脉显影，随后发生实质对比增强。

对于动脉显影，**碘的输送速率**起着关键作用。

在评估实体器官（例如肝脏或胰腺）时，实质器官增强主要取决于给予的**碘总量**，因为病变的显影可能需要注射更大体积的对比剂。

静脉注射 RCM 的应用：

- 计算机断层扫描
- 数字减影血管造影
- 静脉尿路造影
- 静脉造影术
  - 下腔静脉及其属支
  - 上腔静脉及其属支
  - 四肢
- 其他静脉部位
  - 硬膜外静脉造影

The **timing of image acquisition**, relative to the time of injection of the contrast agent, has an impact on which anatomic structures have accumulated the greatest concentration of the administered RCM and thus can be optimally visualised.

Five phases of contrast enhancement for CT imaging:

Non-enhanced phase: imaging prior to RCM injection: determination of the baseline status of the anatomy and detection of calcified structures (e.g., calculi, vascular calcifications, and dystrophic calcification in some tumours).

Early arterial phase: image acquisition a few seconds after bolus administration of intravenous RCM: detection of arterial abnormalities (e.g., arterial dissections).

Late arterial phase: image acquisition 15 to 20 seconds after the early arterial phase: examination of highly vascularised anatomic structures (e.g., liver, spleen, kidneys), especially for the identification of well-vascularized masses.

Portal venous phase: later phase of image acquisition, when the RCM is maximally concentrated in the mesenteric venous structures: assessing liver perfusion, examining cirrhotic patients for portal hypertension.

Delayed phase or wash out phase or the equilibrium phase: visualisation of lesions that present a slower RCM uptake, or in order to characterize slow wash-out kinetics (e.g. tumours).

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章节大纲：

相对于对比剂注射时间，**图像采集时间**会影响所注射的 RCM 在哪些解剖结构中蓄积浓度最高，进而影响哪些结构可被最佳显影。

CT 成像的五个对比增强时相：

非增强期：RCM 注射前成像：用于确定解剖结构的基线状态及检测钙化结构（如结石、血管钙化及部分肿瘤的营养不良性钙化）。

动脉早期：静脉推注 RCM 后数秒内采集图像，用于检测动脉异常（如动脉夹层）。

动脉晚期：在动脉早期后 15 至 20 秒进行图像采集，用于检查高血管化的解剖结构（如肝、脾、肾），尤其适用于识别富血管肿块。

门静脉期：RCM 在肠系膜静脉结构中浓度达峰值的后期成像，用于评估肝脏灌注、检查肝硬化患者是否存在门静脉高压。

延迟期/廓清期/平衡期：用于显示 RCM 摄取较慢的病灶，或为了表征缓慢廓清动力学（例如肿瘤）。

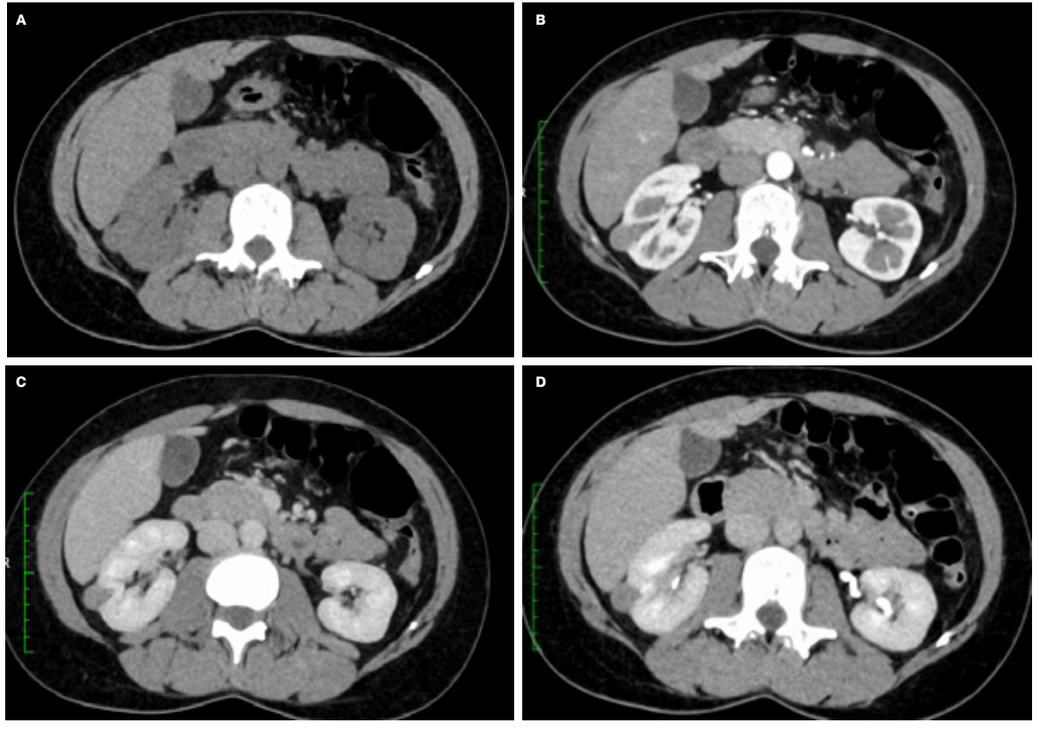

FIGURE 18

Example of a CT of the abdomen with different phases of contrast enhancement. **A**. Non-enhanced phase. **B**. Arterial phase. **C**. Venous phase. **D**. Late phase. Case courtesy: Thomas de Perrot, MD, University Hospitals Geneva.

Contrast Agents

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章节大纲：

图 18

腹部 CT 不同对比增强时相的示例。**A**. 非增强期。**B**. 动脉期。**C**. 静脉期。**D**. 晚期。病例提供：日内瓦大学医院医学博士，Thomas de Perrot。

Intraarterial RCM Injection

Intraarterial injection is the primary method of iodinated RCM delivery used in **diagnostic catheter angiography and catheter-directed arterial intervention**, such as percutaneous angioplasty and stent placement.

High rates of RCM administration combined with a selective approach are required to opacify the target vessels due to the high arterial flow rate.

Applications of intraarterial RCM administration:

- Angiocardiography
- Computed tomography angiography
- Coronary angiography
- Pulmonary angiography
- Aortography
- Visceral and peripheral arteriography
- Digital subtraction angiography
- Vascular pathologies of the central nervous system
- Cerebral, vertebral and spinal angiography

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章节大纲：

动脉内 RCM 注射

在诊断性导管血管造影和导管引导的动脉介入治疗（如经皮血管成形术和支架置入术）中，动脉内注射是碘化 RCM 的主要给药方式。

由于动脉血流速度较快，为使目标血管显影，需要采用高流速注射 RCM，并结合选择性给药方法。

动脉内注射 RCM 的应用：

- 心血管造影
- 计算机断层扫描血管造影
- 冠状动脉造影
- 肺血管造影
- 主动脉造影
- 内脏和外周动脉造影
- 数字减影血管造影
- 中枢神经系统血管病变
- 脑、脊椎和脊髓血管造影

Oral and Rectal RCM Applications

Oral or rectal contrast media are utilised in a variety of ways for imaging of the gastrointestinal tract, which is predominantly done with barium sulfate suspensions and, in selected cases, with iodinated contrast media.

Barium Sulfate

For radiographic imaging of the gastrointestinal tract, barium sulfate suspension is administered orally, rectally or instilled into an enterostomy tube or catheter, and is employed to fill the gastrointestinal tract lumen or to coat the mucosal surface.

Improved delineation of the gastrointestinal tract lumen and mucosa may be achieved by double-contrast examination with filling of the lumen with gas and coating of the wall with barium sulfate (**Fig. 19, see next page**). For this purpose, barium sulfate administration is followed by a gel, carbon dioxide or a gas-forming agent or air might get insufflated through the enema tube.

Barium sulfate is neither absorbed nor metabolised in subjects with a normal gastrointestinal tract and is excreted unchanged in the faeces.

Indications of barium sulfate in radiographic imaging include differentiation of morphological structures, especially between normal and pathological tissue, as well as functional changes through the entire gastrointestinal tract.

口服和直肠 RCM 应用

口服或直肠对比剂以多种方式用于胃肠道成像，主要使用硫酸钡混悬液，在某些情况下使用碘对比剂。

硫酸钡

用于胃肠道放射成像时，硫酸钡混悬液可通过口服、直肠给药或经造瘘管/导管注入，用于充盈胃肠道管腔或涂布黏膜表面。

通过向管腔充入气体使管壁涂布硫酸钡的双重对比检查，可更好地显示胃肠道管腔和黏膜（**见图 19，下页**）。为此，在给予硫酸钡后，可通过灌肠管注入凝胶、二氧化碳、产气剂或空气。

在胃肠道正常的个体中，硫酸钡既不被吸收也不被代谢，而是以原形随粪便排出。

硫酸钡在放射成像中的**适应证**包括区分形态结构，尤其是正常组织与病理组织之间的区分，以及显示整个胃肠道的功能变化。

Adverse Reactions

The most common adverse reactions of barium sulfate include nausea, vomiting and abdominal cramping or discomfort during and after the examination and mild allergic reactions. The hypoosmolality of the suspension causes water withdrawal from the GI tract, which can lead to colon obstruction.

The most serious complication from the use of barium sulfate in the GI tract is leakage into the mediastinum or peritoneal cavity, leading to persistent peritonitis or mediastinitis.

<!> ATTENTION

Contraindications

Contraindications for barium sulfate include suspected perforation and postoperative insufficiency of suture as well as previous allergic reactions to barium products.

Barium sulfate should not be used in individuals who are suspected or known to suffer from necrotic colitis, ileus and deglutition difficulties due to the risk of aspiration, and particular caution is required for newborns, elderly and critically ill persons.

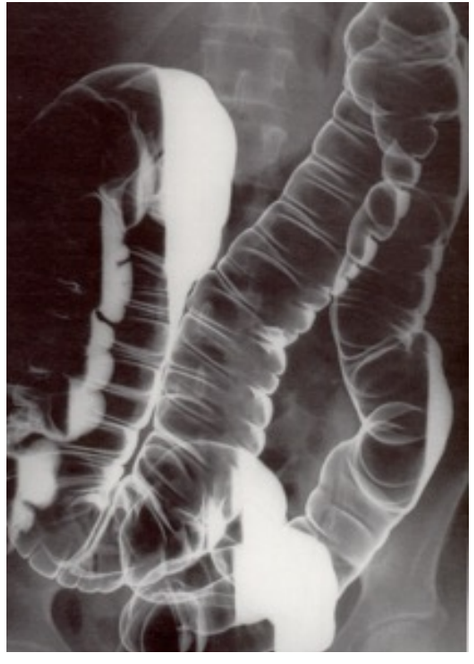

FIGURE 19

Colon with barium sulfate followed by a gel: double contrast image.

Contrast Agents

CHAPTER OUTLINE:

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章节大纲：

不良反应

硫酸钡最常见的不良反应包括检查期间和检查后的恶心、呕吐和腹部痉挛性绞痛或不适以及轻度过敏反应。混悬液的低渗性会导致胃肠道水分流失，可能引发结肠梗阻。

在胃肠道使用硫酸钡时，最严重的并发症是钡剂漏入纵隔或腹膜腔，导致持续性腹膜炎或纵隔炎。

<!> 注意

禁忌证

硫酸钡的禁忌证包括疑似穿孔、术后缝合不全以及既往对钡剂产品过敏。

由于存在误吸风险，硫酸钡不应在疑似或确诊坏死性结肠炎、肠梗阻及吞咽困难的个体中使用，新生儿、老年人及危重症患者需特别谨慎。

图 19

结肠内注入硫酸钡后再注入凝胶：双重对比图像。

Oral Iodinated RCM

The current applications of oral iodinated RCM (**Fig. 20**) are primarily limited to visualisation of the GI tract when barium sulfate is contraindicated.

Diluted water-soluble ionic high-osmolality RCM are preferred for oral use, but diluted non-ionic contrast agents can also be employed.

Water-soluble contrast media are absorbed rapidly from the interstitial spaces and peritoneal cavity, which makes them uniquely useful in examining patients with a suspected hollow viscus perforation. No permanent deleterious effects from the presence of water-soluble contrast media in the mediastinum, pleural cavity or peritoneal cavity have been reported.

Excretion of orally administered iodinated RCM occurs mainly through the faecal route and is dependent on GI transit time, while only a small volume of iodinated RCM is absorbed from the GI tract and subsequently excreted into the urinary tract.

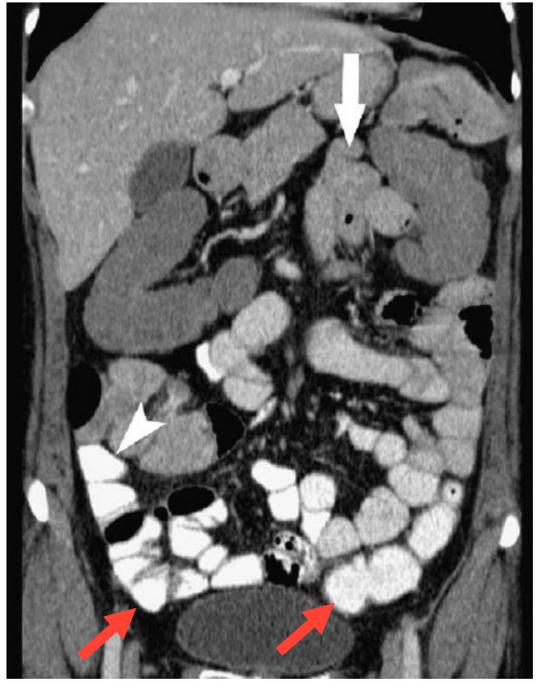

FIGURE 20

CT with oral iodinated RCM. Note the heterogenous contrast in the small bowel with higher iodine concentration in the distal part (**red arrows**).

Contrast Agents

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章节大纲：

口服碘化 RCM

目前口服碘化 RCM 的应用（**图 20**）主要限于硫酸钡禁忌时的胃肠道显影。

口服时首选稀释的水溶性离子型高渗 RCM，但也可采用稀释的非离子型对比剂。

水溶性对比剂可迅速从组织间隙和腹膜腔吸收，这使其在检查疑似空腔脏器穿孔患者时具有独特优势。目前尚无关于水溶性对比剂在纵隔、胸腔或腹腔中存在会产生永久性有害影响的报道。

口服碘化 RCM 主要通过粪便途径排泄，排泄情况取决于胃肠道运输时间，而仅有少量碘化 RCM 从胃肠道吸收，随后排入尿路。

图 20

使用口服碘化 RCM 进行 CT 检查。注意小肠内对比剂分布不均，远端碘浓度较高（**红色箭头**）。

Contraindications

Hyperosmolal RCM may lead to **deglutition difficulties** and are, therefore, contraindicated for oral administration in patients at **risk for aspiration**. In such patients, non-ionic low-osmolality or iso-osmolality iodinated RCM should be used for oral administration because, even if aspirated, they are associated with only minimal bronchogenic toxicity.

Enteric hyperosmolal RCM should also be avoided in patients with **fluid and electrolyte imbalances**, particularly the very young or elderly patients with hypovolemia or dehydration.

Due to a **slight systemic uptake** of orally administered RCM, a careful use is indicated in case of pregnancy, renal insufficiency and underlying thyroid disorder.

Contrast Agents

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章节大纲：

禁忌证

高渗性 RCM 可能导致**吞咽困难**，因此，对于有**误吸风险**的患者，禁忌口服给药。这类患者应使用非离子型低渗或等渗碘化 RCM 口服给药，因为即使误吸，支气管毒性也很小。

对于存在**体液和电解质失衡**的患者，尤其是低血容量或脱水的幼儿或老年患者，也应避免使用**肠道高渗性** RCM。

由于口服 RCM 存在**轻微的全身吸收**，因此在妊娠、肾功能不全和基础甲状腺疾病的情况下应谨慎使用。

/ Adverse Reactions to RCM

<!> ATTENTION

The incidence of adverse reactions related to the intravascular administration of iodinated RCM, which has been **drastically reduced** with the change in usage from ionic high-osmolality RCM to non-ionic low-osmolality or iso-osmolality RCM, is now **generally low**.

Acute Adverse Reactions

Acute adverse reactions to RCM occur **within 1 hour** after application, and the severity of such reactions can range from mild to severe and life-threatening. Acute reactions are categorised as either hypersensitivity reactions and allergy-like reactions, or chemotoxic reactions.

Hypersensitivity and allergic-like reactions are likely **independent of dose and concentration** of the RCM and tend to be **unpredictable**.

Symptoms of hypersensitivity and allergic-like reactions include urticaria, pruritis, cutaneous edema, itching and diffuse erythema. Severe acute reactions typically manifest as facial and laryngeal edema, hypotension, bronchospasm and dyspnea, up to hypotensive shock and respiratory or cardiac arrest.

FIGURE 21

Illustration of a hypersensitivity maculopapular reaction due to contrast media.

/ Contrast Agents

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章节大纲：

/ RCM 的不良反应

<!> 注意

从离子型高渗 RCM 转为使用非离子型低渗或等渗 RCM 后，与血管内注射碘化 RCM 相关的不良反应发生率已**大幅降低，目前总体处于较低水平**。

急性不良反应

RCM 的急性不良反应在用药后 **1 小时内**发生，严重程度从轻度到重度不等，甚至危及生命。急性反应分为超敏反应和过敏样反应或化学毒性反应。

超敏反应和过敏样反应可能与 RCM **剂量和浓度无关，并且往往无法预测**。

超敏反应和过敏样反应的症状包括荨麻疹、瘙痒、皮肤水肿、发痒和弥漫性红斑。重度急性反应通常表现为面部和喉水肿、低血压、支气管痉挛和呼吸困难，直至低血压休克和呼吸或心脏骤停。

图 21

对比剂所致超敏性斑丘疹反应的图示。

<!> ATTENTION

Chemotoxic adverse reactions relate to a **specific molecular attribute** of the RCM such as its **chemical structure, osmolality, viscosity and ionicity, and they are generally dose and concentration dependent**.

Common chemotoxic adverse reactions include nausea and vomiting, flushing, warmth, chills, headache, dizziness, anxiety, taste alterations and hypertension. Vasovagal reactions can occur and appear as bradycardia with hypotension.

Serious chemotoxic adverse reactions can manifest as cardiac arrhythmias, depressed myocardial contractility, cardiogenic pulmonary edema, convulsions and seizures. They are more frequent and significant in patients with **underlying cardiac disease**.

Patient-related **risk factors** for an acute reaction to RCM are a history of a previous allergic-like reaction to a contrast agent and a history of asthma and atopy, while contrast medium related risk factors are high-osmolality ionic contrast media.

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<!> 注意

化学毒性不良反应与 RCM 的**特定分子属性**有关，例如其**化学结构、渗透压、黏度和离子性，并且通常具有剂量和浓度依赖性**。

常见的化学毒性不良反应包括恶心和呕吐、潮红、温热、寒战、头痛、头晕、焦虑、味觉改变和高血压。可能出现血管迷走神经反应，表现为心动过缓伴低血压。

严重化学毒性不良反应可表现为心律失常、心肌收缩力下降、心源性肺水肿、惊厥和癫痫发作。在有**基础心脏疾病**的患者中，这些不良反应更为常见且严重。

RCM 急性反应的患者相关风险因素为既往对比剂过敏样反应史以及哮喘和特应性过敏体质病史，而对比剂相关风险因素为高渗性离子型对比剂。

<!> ATTENTION

Delayed Adverse Reactions

Delayed adverse reactions may develop from 60 minutes to up to one week following RCM exposure and are most commonly but not limited to cutaneous reactions.

Typical delayed cutaneous reactions can manifest as rashes, pruritus, erythema and swelling, while delayed non-cutaneous symptoms include nausea, vomiting, headache, musculoskeletal pain, diarrhea and, occasionally, hypotension.

Risk factors for a delayed reaction to RCM are a previous late contrast medium reaction and a treatment with interleukin-2, as well as use of non-ionic dimers.

Pregnancy and lactation

In pregnant women, when radiographic examination is essential, iodine-based contrast media may be given. Following such administration, the thyroid function should be checked in the neonate during the first week and monitored for the first three years.

Breast feeding may be continued normally when iodine-based contrast media is given to the mother.

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<!> 注意

迟发性不良反应

迟发性不良反应可能在 RCM 暴露后 60 分钟至一周内发生，最常见但不限于皮肤反应。

典型的迟发性皮肤反应可表现为皮疹、瘙痒、红斑和肿胀，而迟发性非皮肤症状包括恶心、呕吐、头痛、肌肉骨骼疼痛、腹泻，偶见低血压。

RCM 迟发性反应的风险因素包括既往对比剂迟发反应史、白细胞介素-2 治疗史，以及使用非离子型二聚体对比剂。

妊娠期与哺乳期

妊娠女性如必须进行影像学检查，可使用含碘对比剂。使用后，应在新生儿出生后第一周检查甲状腺功能，并在头三年内进行监测。

哺乳期女性使用含碘对比剂后，可正常继续母乳喂养。

<!> ATTENTION

Thyrotoxicosis

A contributing factor to adverse reactions is the **deiodination process and iodide impurity** in the solutions thus leading to traces of free iodide in the body with concentrations above the recommended daily intake.

In subjects with a normal thyroid function, the exposure with excess iodide can be compensated by a transient decrease of thyroid hormone synthesis, the so-called Wolff-Chaikoff effect.

This intrinsic regulatory mechanism is impaired in subjects with an underlying thyroid disorder, so that the application of iodinated contrast media may lead to a thyrotoxicosis.

FIGURE 22

Light exposure might lead to a deiodination with iodide release.

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<!> 注意

甲状腺毒症

不良反应的一个影响因素是**脱碘过程和溶液中的碘化物杂质**，这会导致体内游离碘化物的痕量浓度超过每日推荐摄入量。

在甲状腺功能正常的个体中，过量碘化物暴露可通过甲状腺激素合成的短暂减少来代偿，即所谓的 Wolff-Chaikoff 效应。

基础甲状腺疾病患者的这种内在调节机制受损，因此使用碘化对比剂可能导致甲状腺毒症。

图 22

光照可能导致脱碘并释放碘化物。

<!> ATTENTION

Risk factors for development of **thyrotoxicosis** are Graves' disease and multinodular goiter with thyroid autonomy, especially in elderly individuals and/or in areas of dietary iodine deficiency.

For individuals suspected of being at risk of thyrotoxicosis, knowledge of thyroid function before administration of iodinated RCM is helpful, and close monitoring after administration is recommended. Selected high-risk patients may benefit from prophylactic thyrostatic therapy.

In patients with established **hyperthyroidism**, administration of iodinated contrast media is contraindicated.

Following administration of iodine-based contrast media to a pregnant woman, thyroid function should be checked in the neonate during the first week.

Premature infants and **neonates** might be particularly susceptible to developing clinically significant **hypothyroidism** because the immature gland may not be able to fully reverse the acute Wolff-Chaikoff effect. Thyroid function should be monitored up to the age of three.

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章节大纲：

<!> 注意

发生**甲状腺毒症**的风险因素为格雷夫斯病和伴有甲状腺自主性的多结节性甲状腺肿，特别是在老年人和/或饮食碘缺乏地区人群中。

对于疑似存在甲状腺毒症风险的患者，有必要在给予碘化 RCM 前了解甲状腺功能，并建议在使用后进行密切监测。部分高危患者可能受益于预防性甲状腺抑制治疗。

确诊**甲状腺功能亢进**的患者禁用碘化对比剂。

孕妇使用含碘对比剂后，应在新生儿出生后第一周检查其甲状腺功能。

早产儿和**新生儿**可能特别容易发生有临床意义的**甲状腺功能减退症**，因为未成熟的甲状腺腺体可能无法完全逆转急性 Wolff-Chaikoff 效应。应监测甲状腺功能直至 3 岁。

<!> ATTENTION

Renal Adverse Reactions

Intravascular administration of a contrast medium may result in a deterioration of the renal function and even in acute kidney failure.

The **standard diagnostic criterion** for Post-Contrast Acute Kidney Injury (PC-AKI) is defined as an increase in serum creatinine by > 0.3 mg/dl (or > 26.5 µmol/l), or to > 1.5 times baseline within 48-72 hours of intravascular administration of a contrast medium.

A **preexisting renal dysfunction** is the greatest risk factor for developing PC-AKI, and the risk becomes larger with increasing baseline renal impairment.

The estimated glomerular filtration rate (eGFR), calculated from the serum creatinine, is the recommended parameter to estimate renal function before contrast medium administration. The current guidelines of the **European Society of Urogenital Radiology (ESUR)** define the following threshold values for patient related risk of developing PC-AKI:

eGFR < 45 ml/min/1.73 m²

before intraarterial contrast medium administration with first pass renal exposure or in intensive care unit patients.

eGFR < 30 ml/min/1.73 m²

before intravenous contrast medium or intra-arterial contrast medium administration with second pass renal exposure.

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<!> 注意

肾脏不良反应

血管内注射对比剂可能导致肾功能恶化，甚至导致急性肾衰竭。

对比剂后急性肾损伤（Post-Contrast Acute Kidney Injury，PC-AKI）的**标准诊断标准**为：血管内注射对比剂后 48～72 小时内，血清肌酐升高 > 0.3 mg/dL（或 > 26.5 µmol/L），或升至基线值的 1.5 倍以上。

既存肾功能不全是发生 PC-AKI 的最大风险因素，且基线肾功能损害程度越重，风险越大。

根据血清肌酐计算的估计肾小球滤过率（estimated glomerular filtration rate，eGFR）是推荐用于对比剂注射前评估肾功能的参数。**欧洲泌尿生殖放射学会（European Society of Urogenital Radiology，ESUR）**的现行指南针对患者发生 PC-AKI 的风险定义了以下阈值：

eGFR < 45 mL/min/1.73 m²

在经肾首次暴露的动脉内注射对比剂前，或在重症监护病房患者中使用对比剂前。

eGFR < 30 mL/min/1.73 m²

在静脉注射对比剂或经肾二次暴露的动脉内注射对比剂前。

In their Manual on Contrast Media 2024, the ACR Committee on Drugs and Contrast Media of the American College of Radiology, mention the following threshold value for patient related risk of developing PC-AKI:

eGFR < 30 ml/min/1.73 m^2

Contrast Agents

对比剂

美国放射学会（American College of Radiology，ACR）药物与对比剂委员会在其《2024 年对比剂手册》中提到了与患者发生 PC-AKI 风险相关的以下阈值：

eGFR < 30 mL/min/1.73 m^2

<▪> CORE KNOWLEDGE

Further risk factors for developing PC-AKI include diabetes mellitus, cardiovascular disease, hypertension, hyperuricemia, proteinuria, diuretic use, dehydration, advanced age and multiple iodinated contrast medium doses administered in a short time interval.

Preventive strategies comprise 1-12 hours of prehydration with intravenous saline or sodium bicarbonate followed by 4-12 hours of posthydration and the use of low- or iso-osmolal RCM with the minimum dose.

<▪> 核心知识

发生 PC-AKI 的其他风险因素包括糖尿病、心血管疾病、高血压、高尿酸血症、蛋白尿、使用利尿剂、脱水、高龄，以及短时间内多次使用碘化对比剂。

预防策略包括静脉输注生理盐水或碳酸氢钠进行 1～12 小时的预先水化，随后进行 4～12 小时的后续水化，并使用最低剂量的低渗或等渗 RCM。

Extravasation

An unintended extravascular injection of iodinated RCM occurs in very **rare cases only** and typically causes self-limiting symptoms such as pain, erythema and swelling, but in severe cases, skin ulceration and necrosis may occur. The most commonly reported severe injury after extravasation is the development of the compartment syndrome.

A severe extravasation injury is more likely to result in patients with arterial insufficiency or compromised venous or lymphatic drainage in the affected extremity.

Extravasations involving larger volumes of RCM, especially high-osmolality and high-viscosity agents, or the use of a power injector, and those occurring at problematic injection sites such as the dorsum of the hand, foot or ankle, are more likely to result in severe tissue injury.

Continuous monitoring and accurate conservative management help to avoid sequelae. The treatment consists in elevation of the affected extremity, ice cooling, topical application of silver sulfadiazine and, in extreme cases, surgical intervention.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

外渗

碘化 RCM 意外血管外注射**的情况非常罕见**，通常会导致疼痛、红斑和肿胀等自限性症状，但在严重情况下可能发生皮肤溃疡和坏死。外渗后最常见的严重损伤是发生骨筋膜室综合征。

对于患肢存在动脉供血不足或静脉/淋巴回流障碍的患者，发生严重外渗损伤的可能性更高。

若外渗涉及较大量的 RCM（尤其是高渗、高黏度对比剂），或使用动力注射器注射，或发生在手背、足背、踝关节等易出现问题的注射部位时，更易导致严重组织损伤。

持续监测和准确的保守治疗有助于避免后遗症。治疗方法包括抬高患肢、冰敷、局部使用磺胺嘧啶银，在极端情况下需进行手术干预。

Magnetic Resonance Contrast Agents

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

磁共振对比剂

/ Magnetic Resonance Contrast Agents

Magnetic resonance imaging (MRI) contrast agents are diagnostic pharmaceutical compounds that affect the **nuclear magnetic resonance signal of the 1H-hydrogen nuclei (protons) of water molecules** contained in the surrounding tissue.

The contrast of an MR image results from a complex interplay of various factors such as proton density, the longitudinal (spin-lattice) relaxation time T1 and the transverse (spin-spin) relaxation time T2, and on the applied MRI sequences.

Contrast agents (CAs) used in MRI either consist of **paramagnetic metal ions or of superparamagnetic particles**, and they act to modify T1 and T2 of water protons present in the tissue.

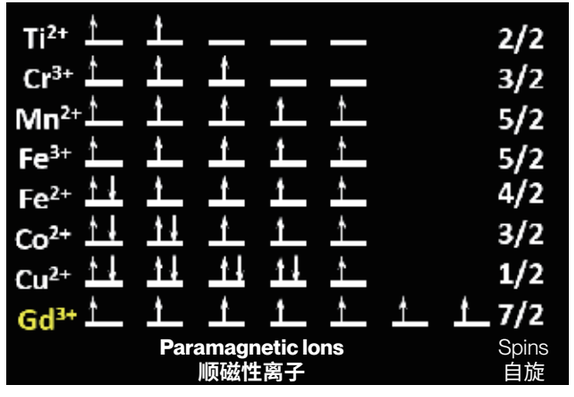

FIGURE 23

Single spins (here electrons) are magnetised in the MR and interact with protons thus changing the tissue signal.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 磁共振对比剂

磁共振成像（Magnetic resonance imaging，MRI）对比剂是一种诊断性药物化合物，可影响**周围组织中所含水分子的 1H-氢核（质子）的磁共振信号**。

MR 图像的对比度源于多种因素的复杂相互作用，诸如质子密度、纵向（自旋-晶格）弛豫时间 T1 和横向（自旋-自旋）弛豫时间 T2 以及所应用的 MRI 序列。

MRI 中使用的对比剂（Contrast agent，CA）**由顺磁性金属离子或超顺磁性颗粒**组成，其作用是改变组织中水质子的 T1 和 T2 弛豫时间。

图 23

在 MR 中，单个自旋（此处指电子）会被磁化并与质子相互作用，从而改变组织信号。

/ Paramagnetic Contrast Agents

Paramagnetic CAs contain metal ions that have unpaired electrons in their outer shell, which implies a resultant electron spin and a permanent magnetic moment.

The magnetic moment of a tumbling paramagnetic CA molecule induces an additional, time-variable magnetic field in the hydrogen nuclei of the surrounding water molecules, which in turn can increase the rate r1 of longitudinal spin-lattice relaxation and the rate r2 of transverse spin-spin relaxation.

The increase in relaxation rate caused by a CA leads to a corresponding shortening of T1 and T2 in the region of interest, producing hyperintense signals in T1-weighted images and hypointense signals in T2-weighted images.

The effect on T1 is already evident at low concentrations of the contrast agent, whereas the effect on T2 becomes increasingly significant at higher concentrations.

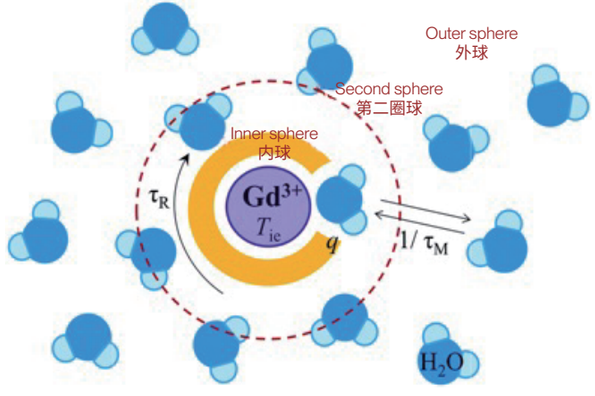

FIGURE 24

Gadolinium interacting with the surrounding water protons at different levels. Usually 1-2 water protons get closer to the central atom surrounded by a ligand (inner-sphere interaction). With newer agents the number of interacting protons can double allowing direct interaction of 2 water molecules (q-factor of 2 instead of 1).

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 顺磁性对比剂

顺磁性 CA 含有外壳中存在未配对电子的金属离子，这意味着会产生电子自旋和永久磁矩。

翻滚的顺磁性 CA 分子的磁矩在周围水分子的氢核中感应一个额外的时变磁场，这继而可增加纵向自旋-晶格弛豫速率 r1 和横向自旋-自旋弛豫速率 r2。

CA 引起的弛豫速率增加导致目标区域的 T1 和 T2 相应缩短，在 T1 加权图像中产生高信号，在 T2 加权图像中产生低信号。

对比剂在低浓度时对 T1 的影响已较为明显，而对 T2 的影响则在较高浓度时愈发显著。

图 24

轧在不同层面与周围水质子相互作用。通常 1~2 个水质子更靠近被配体包围的中心原子（内球相互作用）。对于较新型的对比剂，相互作用的质子数可翻倍，从而使 2 个水分子直接相互作用（q 因子从 1 变为 2）。

Relaxivity

The efficacy of a MR contrast agent is expressed in terms of relaxivity R, which refers to the ability of the CA to enhance the proton relaxation rate. It is generally measured experimentally in water and is defined as the increase in relaxation time of the solvent (water) induced by 1 mmol L–1 of the active ion of the contrast agent:

$$R_1 = 1 / T_1 \text{ (1 Mol, 20°C)}$$

The contrast efficiency is expressed as the r2/r1 ratio: the higher the ratio, the greater the relative effect on T2 and vice versa on T1.

Manganese-Based Contrast Agents

Manganese-based CAs contain bivalent manganese, a transition metal with five unpaired electrons, which is also naturally present in the body.

Paramagnetic manganese is available either in the form of small molecules or as the more recently developed nanometre sized materials.

Mangafodipir trisodium (Mn-DPDP) is a liver specific CA in which a manganese ion Mn^{2+} is chelated with a dipyridoxyldiphosphate ligand.

	GADOPICLENOL	GADOTERATE	GADOBUTROL	GADOTERIDOL	GADOBENATE	GADODIAMIDE	GADOPENTETATE
Relaxivity $mM^{-1}s^{-1}$ in water 37°C, 1.5T	12.2/15.0	2.9 / 3.2	3.3 / 3.9	2.9 / 3.2	4.0 / 4.3	3.3 / 3.6	3.3 / 3.9
Dosing in mmol Gd per kg BW	0.05	0.1	0.075 (CNS) and 0.1	0.1	0.1	0.1	0.1

TABLE 2

Doses: The higher relaxivities of certain agents allow to adapt the dosing in mmols per kg body-weight in clinical routine. This permits to reduce the gadolinium exposition of the patient.

Robic C et al. Invest Radiol. 2019

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

弛豫率

MR 对比剂的效能以弛豫率 R 表示，弛豫率是指 CA 增强质子弛豫速率的能力。弛豫率通常在水中通过实验测量，定义为 1 mmol/L 对比剂活性离子引起的溶剂（水）弛豫时间增加量：

$$R_1 = 1 / T_1 \text{ (1 Mol, 20°C)}$$

对比效率以 r2/r1 比值表示：该比值越高，对 T2 的相对影响越大，反之则对 T1 的影响越大。

含锰对比剂

含锰 CA 含有二价锰，这是一种具有五个未配对电子的过渡金属，也天然存在于体内。

顺磁性锰既可以小分子形式存在，也可以近年来开发的纳米级材料形式存在。

锰福地吡三钠 (Mn-DPDP) 是一种肝脏特异性 CA，其中锰离子 Mn^{2+} 与双吡啶氧基二磷酸配体螯合。

	钆哌啶醇	钆特酸	钆布醇	钆特醇	钆贝酸	钆双胺	钆喷酸
弛豫率 $mM^{-1}s^{-1}$ 水溶液，37°C，1.5T	12.2/15.0	2.9/3.2	3.3/3.9	2.9/3.2	4.0/4.3	3.3/3.6	3.3/3.9
剂量 (mmol Gd/kg BW)	0.05	0.1	0.075 (CNS) 和 0.1	0.1	0.1	0.1	0.1

表 2

剂量：某些对比剂的弛豫率较高，因此能够在临床常规中按每公斤体重的毫摩尔数调整给药剂量。这样可以减少患者的钆暴露。

Robic C et al. Invest Radiol. 2019

/ Gadolinium-Based Contrast Agents

Gadolinium-based CAs, which contain trivalent gadolinium – a metal from the lanthanide series with seven unpaired electrons – **are the most clinically used CAs in MRI** because of their high magnetic moment and long electronic spin relaxation time.

However, the cytotoxicity of gadolinium in its free ionic form Gd^{3+} makes it necessary to mask the gadolinium by providing **chelating ligands** which form chemically stable complexes.

Administering gadolinium as an inert and stable coordination complex prevents the cellular uptake of free Gd^{3+} and maintains the biodistribution within the extracellular space, thereby enhancing renal filtration and urinary excretion.

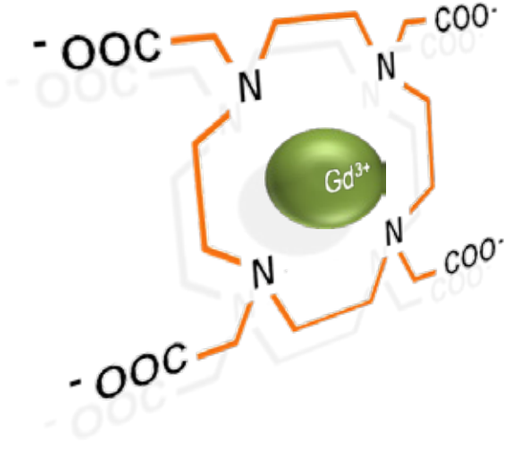

FIGURE 25

Macrocyclic gadolinium complex with Gd^{3+} as the central atom bound tightly to a ligand presenting a ring-like structure.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 含钆对比剂

含钆 CA 含有三价钆（一种镧系金属，有 7 个未配对电子），由于其具有高磁矩和较长的电子自旋弛豫时间，成为 **MRI 中临床应用最广泛的 CA**。

然而，游离离子形式$^{3+}$ 的钆具有细胞毒性，因此必须通过提供能形成化学稳定复合物的**螯合配体**来掩蔽钆。

将钆作为惰性且稳定的配位络合物给药，可防止游离钆$^{3+}$ 被细胞摄取，并使其在细胞外空间保持生物分布，从而增强肾脏滤过和尿液排泄。

图 25

以 Gd^{3+} 为中心原子的大环钆络合物与配体紧密结合，呈现环状结构。

Structure of the Gadolinium Complexes

The currently available gadolinium-based contrast agents can be classified into four main categories according to their structure, particularly the nature of the chelating moiety, and to their ionicity.

In **linear complexes**, the gadolinium ion is only partially surrounded by a chain-like structure of the ligand, whereas in **macrocyclic complexes**, the gadolinium ion is enclosed within a cage-like structure formed by the ligand.

Both, the linear and the macrocyclic gadolinium complexes can either be **non-ionic or ionic**. In the ionic gadolinium complexes, the remaining anionic groups are salified with meglumine or sodium cations.

The molecular characteristics of the four classes of gadolinium complexes have a significant impact on some key properties such as **osmolality and viscosity**, but also on their **relaxivity and biodistribution**.

The molecular characteristics are also responsible for the differences between the various gadolinium complexes regarding their **thermodynamic stability constants and kinetic rate constants**.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

钆络合物的结构

目前可用的含钆对比剂根据其结构（尤其是螯合部分的性质）及其离子性可分为四大类。

在**线性络合物**中，钆离子仅被配体的链状结构部分包围，而在**大环络合物**中，钆离子则被配体形成的笼状结构完全包裹。

线性钆络合物和大环钆络合物均可分为**非离子型和离子型**。在离子型钆络合物中，剩余的阴离子基团与葡甲胺或钠离子形成盐。

这四类钆络合物的分子特性不仅对**渗透压和黏度**等关键性质有显著影响，还会影响其**弛豫率和生物分布**。

这些分子特性也是不同钆络合物在**热力学稳定常数和动力学速率常数**方面存在差异的原因。

Stability of Gadolinium Complexes

In solutions of gadolinium-containing CAs, there is always an equilibrium between complexed gadolinium (Gd-Ligand) and free gadolinium ions (Gd^{3+}):

$$Gd^{3+} + Ligand \leftrightarrow Gd\text{-}Ligand$$

The equilibrium state can be characterised by the thermodynamic stability constant:

$$K_{TD} = \frac{[Gd\text{-}Ligand]}{[Gd^{3+}] \cdot [Ligand]}$$

which is often expressed in logarithmic form log KTD. For the gadolinium complexes used as contrast agents, this equilibrium strongly favors the side of the complexed gadolinium, with log KTD ranging from 16.9 to 25.6.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

钆络合物的稳定性

在含钆 CA 溶液中，络合钆（Gd-配体）和游离钆离子 (Gd^{3+}) 之间始终存在平衡：

$$Gd^{3+} + 配体 \leftrightarrow Gd\text{-}配体$$

这种平衡状态可用热力学稳定常数来表征：

$$K_{TD} = \frac{[Gd\text{-}配体]}{[Gd^{3+}] \cdot [配体]}$$

该常数通常以对数形式 log KTD 表示。对于用作对比剂的钆络合物，这种平衡强烈倾向于络合钆一侧，其 log KTD 值范围为 16.9 至 25.6。

COMPLEXES	STRUCTURE	THERMODYNAMIC STABILITY -LOG K	KINETIC STABILITY AT PH 7.4	DISSOCIATION HALF-LIFE AT 25°C, PH 1.0
Gadopiclenol	macrocyclic, non-ionic	18.7	high	20 days+/-3d
Gd-DOTA	macrocyclic, ionic	25.6	high	338 hours
Gd-HP-DO3A	macrocyclic, non-ionic	23.8	high	3.9 hours
Gd-BT-DO3A	macrocyclic, non-ionic	21.8	high	43 hours
Gd-BOPTA	inear-ionic	22.6	medium	< 5 sec
Gd-DTPA	linear-ionic	22.1	low	< 5 sec
Gd-DTPA-BMA	linear-non-ionic	16.9	low	< 5 sec

TABLE 3

Stability of gadolinium complexes

Robic C et al. Invest Radiol. 2019

The thermodynamic stability of gadolinium complexes decreases with **decreasing pH**, so that in acidic environment the complexes are more prone to decomplexation.

Macrocyclic complexes generally have a **higher** thermodynamic and kinetic stability than linear complexes.

Ionic compounds tend to have a slightly **higher** thermodynamic and kinetic stability than non-ionic compounds.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

络合物	结构	热力学稳定性-LOG K	PH 7.4 下的动力学稳定性	25°C、PH 1.0 下的解离半衰期
钆哌啶醇	大环，非离子型	18.7	高	20 天 ± 3 天
Gd-DOTA	大环，离子型	25.6	高	338 h
Gd-HP-DO3A	大环，非离子型	23.8	高	3.9 h
Gd-BT-DO3A	大环，非离子型	21.8	高	43 h
Gd-BOPTA	线性-离子型	22.6	中	< 5 秒
Gd-DTPA	线性-离子型	22.1	低	< 5 秒
Gd-DTPA-BMA	线性-非离子型	16.9	低	< 5 秒

表 3

钆络合物的稳定性

Robic C et al.Invest Radiol.2019

钆络合物的热力学稳定性随着 **pH 的降低**而降低，因此在酸性环境中，络合物更容易发生解络合。

大环络合物的热力学和动力学稳定性通常**高于**线性络合物。

离子化合物的热力学和动力学稳定性往往略**高于**非离子化合物。

Transmetallation

Decomplexation of the gadolinium complexes may result from **reactions with other metal ions that are present in human body fluids**.

In particular, the Gd^{3+} ion in a chelate complex may be replaced by Zn^{2+}, which leads to release of toxic Gd^{3+} ions and to formation of zinc complexes resulting in an undesirable zinc washout via renal elimination.

An important reason for the toxicity of free Gd^{3+} ions is the size similarity and resulting competition with Ca^{2+} ions in cellular and biochemical processes, leading to an inhibition of calcium channels and a blockage of Ca^{2+} dependent enzymes.

A further factor contributing to the toxicity of Gd^{3+} ions is their tendency to bind to endogenous anions, particularly phosphates and carbonates, creating insoluble salts which are taken up by the reticuloendothelial system (RES) through phagocytosis and accumulating in human tissues (style). This process is accompanied by a stimulation of local macrophages to initiate an inflammatory response with the release of cytokines and cytokine triggered transcription factors.

Contrast Agents

CHAPTER OUTLINE:

金属转移

钆络合物的解络合可能是由于**与人体体液中存在的其他金属离子发生反应**所致。

特别是，螯合络合物中的 Gd^{3+} 离子可被 Zn^{2+} 取代，这会导致释放有毒的 Gd^{3+} 离子并形成锌络合物，从而通过肾脏排泄产生不良的锌清除。

游离 Gd^{3+} 离子具有毒性的一个重要原因是，其与 Ca^{2+} 离子尺寸相似，导致二者在细胞和生化过程中产生竞争，进而抑制钙通道并阻断 Ca^{2+} 依赖性酶的活性。

导致 Gd^{3+} 离子毒性的另一个因素是其倾向于与内源性阴离子（尤其是磷酸盐和碳酸盐）结合，产生不溶性盐，这些盐被网状内皮系统（reticuloendothelial system，RES）通过吞噬作用摄取，并在人体组织中蓄积（形式）。这一过程伴随着局部巨噬细胞的刺激，从而引发炎症反应，释放细胞因子及由细胞因子触发的转录因子。

对比剂

章节大纲：

Pharmacokinetics

After intravenous administration, gadolinium complexes are **rapidly distributed into the intravascular space and then passed**, through the capillaries, **into the interstitial space**, with the intravascular half-life time being dependent on the molecular weight and on the extent of plasma protein binding.

Depending on its structure, a gadolinium complex may also be **partially distributed in the liver** through passive diffusion or through a selective uptake by hepatocytes via carrier-mediated transport across the cell membranes.

Gadolinium contrast agents **do not penetrate the intact blood-brain barrier**.

Low molecular weight gadolinium complexes are generally not metabolised.

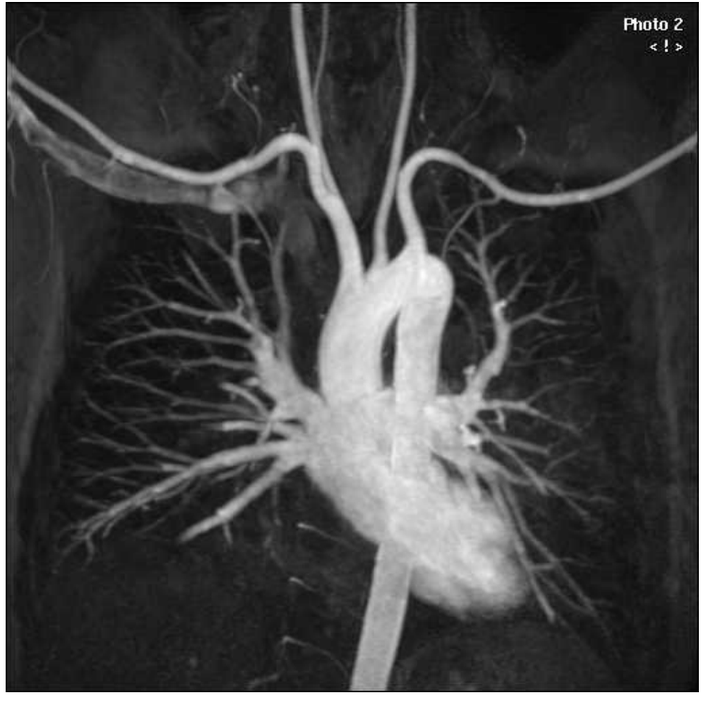

FIGURE 26

Early vascular distribution of the iv injected gadolinium contrast agent.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

药代动力学

静脉注射后，钆络合物**迅速分布至血管内空间，然后通过毛细血管进入组织间隙**，其血管内半衰期取决于分子量及血浆蛋白结合程度。

根据其结构，钆络合物也可能通过被动扩散或通过载体介导的跨细胞膜转运被肝细胞选择性摄取而**部分分布于肝脏**。

钆对比剂**不会穿透完整的血脑屏障**。

低分子量钆络合物通常不被代谢。

图 26

静脉注射钆对比剂的早期血管分布。

The gadolinium complexes are **excreted either almost exclusively via the kidneys**, or they have a **dual elimination** pathway via the kidneys and via the hepatobiliary system in case of liver-specific agents (Gadobenate, Gadoxetate).

Patients with **normal renal function** eliminate more than 90% of low molecular weight gadolinium CAs (non-specific) within the first 12 hours after injection.

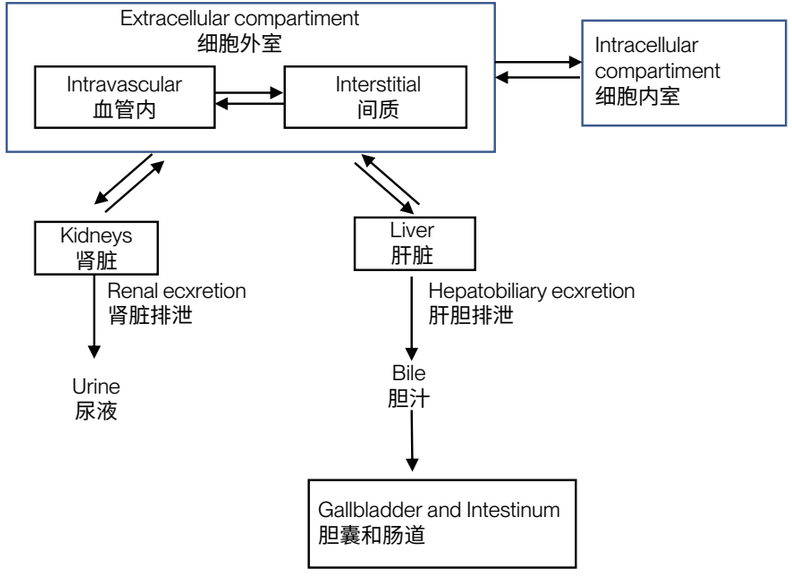

FIGURE 27

Distribution sites and elimination pathways for intravenously administered gadolinium complexes.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

钆络合物**几乎完全通过肾脏排泄**，而对于肝脏特异性对比剂（钆贝酸、钆塞酸），则通过肾脏和肝胆系统的**双重途径代谢**。

肾功能正常的患者在注射后的前 12 小时内可排出超过 90% 的低分子量非特异性钆 CA。

图 27

静脉注射钆络合物的分布部位和消除途径。

/ Superparamagnetic Contrast Agents

Superparamagnetic contrast agents consist of **iron oxide nanoparticle cores** coated with a protective layer of a biocompatible material like polyethylene glycol, dextran, heparin or albumin.

The magnetic moment of the superparamagnetic cores tends to align with the external magnetic field, inducing local magnetic field gradients that dephase the transverse magnetisation of water protons, which predominantly leads to a shortened T_2 and concomitant negative contrast enhancement in pathologically relevant T_2-weighted images. With decreasing size of the superparamagnetic particles, shortening of T_1 becomes more pronounced, so that small superparamagnetic particles with core diameters of less than 10 nm can produce positive contrast in anatomically relevant T_1-weighted images.

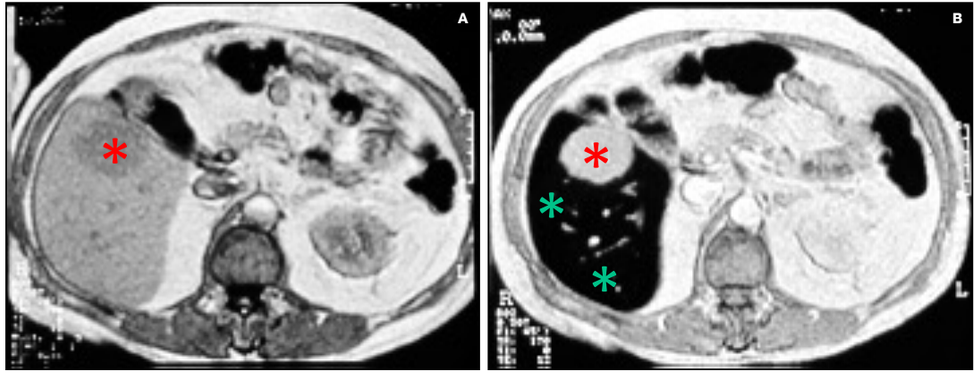

FIGURE 28

Liver MRI pre (A) and post (B) iv administration of iron oxide nanoparticles with no uptake in the hepatocellular carcinoma (red asterisk) and uptake in normal liver tissue (green asterisks).

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 超顺磁性对比剂

超顺磁性对比剂的核心是**氧化铁纳米颗粒**，表面涂有生物相容性材料（如聚乙二醇、葡聚糖、肝素或白蛋白）保护层。

超顺磁核心的磁矩趋于与外部磁场方向一致，从而诱导局部磁场梯度，使水质子的横向磁化失相，这主要会导致 T_2 缩短，并在病理相关的 T_2 加权成像中伴随阴性对比增强。随着超顺磁性颗粒尺寸的减小，其对 T_1 的缩短作用变得更加显著，因此核心直径小于 10 nm 的小尺寸超顺磁性颗粒可在解剖学相关的 T_1 加权成像中产生阳性对比。

图 28

氧化铁纳米颗粒静脉注射前 (A) 和注射后 (B) 的肝脏 MRI，肝细胞癌中无摄取（红色星号），正常肝组织中有摄取（绿色星号）。

/ Indications

MR contrast agents can be classified according to their biodistribution pattern and the consequent applications in the morphological and functional diagnostic practice.

Non-Specific Extracellular Contrast Agents

Extracellular MR contrast agents are **low molecular weight gadolinium complexes** which, after injection, rapidly diffuse from the intravascular space into the extracellular space, from where they are then gradually eliminated by the kidneys.

These contrast agents circulate freely in the extracellular space but do not penetrate into tissues with specialised vascular barriers. Accordingly, they tend to accumulate in **tissues with abnormal perfusion or capillary permeability and in regions where the blood-brain barrier permeability is altered**.

The extracellular MR contrast agents are mainly applied for **CNS examinations** aimed at the detection of various neoplasms, the assessment of demyelinating diseases, infectious and inflammatory processes, the characterisation of vascular anomalies and the diagnosis of cerebral ischemia and infarction. These agents are also **extensively used in body imaging** to asses certain pathologic processes, such as hepatocellular carcinoma or renal cell carcinoma and also for certain muskuloskeletal applications (see next page).

/ 适应证

MR 对比剂可以根据其生物分布模式及其在形态学和功能诊断实践中的应用进行分类。

非特异性细胞外对比剂

细胞外 MR 对比剂是**低分子量钆络合物**，注射后迅速从血管内空间扩散到细胞外空间，然后由肾脏逐渐消除。

这些对比剂可在细胞外空间自由循环，但不会渗透到具有特殊血管屏障的组织中。因此，它们往往会蓄积于**灌注异常或毛细血管通透性异常的组织以及血脑屏障通透性改变的区域**。

细胞外 MR 对比剂主要用于**中枢神经系统 (CNS) 检查**，旨在检测各种肿瘤、评估脱髓鞘疾病、感染和炎症过程、表征血管异常以及诊断大脑缺血和梗死。这些对比剂还**广泛用于体部成像**，以评估某些病理过程，如肝细胞癌或肾细胞癌，也用于某些肌肉骨骼应用（见下页）。

Some extracellular MR contrast agents can also be employed in MR angiography but due to their short residence time in the intravascular space, the imaging acquisition time window is very limited.

For the use as extracellular nonspecific contrast agents, most gadolinium complexes are equally effective because of their similar relaxivities and biodistributions. With the recent introduction of Gadopiclenol offering a higher molar relaxivity per mmol gadolinium the dosing needs to get adapted (0.05 mmol/kg instead of 0.1 mmol/kg bw or 0.075 mmol/kg in case of gadobutrol CNS exams).

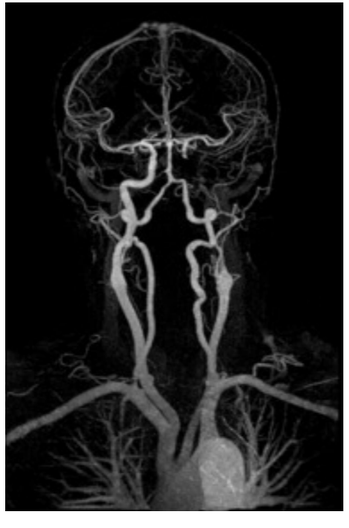

FIGURE 29

Gadolinium-enhanced MRI of the carotid arteries.

<!> ATTENTION

Indications for Non-Specific Extracellular CAs

Central Nervous System

Detection of primary neoplasms and brain metastases, assessment of demyelinating diseases, detection of infectious and inflammatory processes, characterisation of vascular anomalies and diagnosis of cerebral ischemia and infarction.

Abdomen and Pelvis

Detection and characterisation of lesions, and determination of the extent of malignant tumour dissemination.

MR Angiography

Assessment of vascular anatomy and disease.

Breast

Differentiation of malign and benign lesions, detection of multicentric malignancies, recurrent local breast cancer or benign post therapeutic fibrosis.

Musculoskeletal System

Detection and characterisation of mass lesions and inflammatory processes and evaluation of the extent of disease.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

一些细胞外 MR 对比剂也可用于 MR 血管造影，但由于其在血管内空间的停留时间短，成像采集的时间窗口非常有限。

作为细胞外非特异性对比剂使用时，大多数钆络合物具有相同的弛豫率和生物分布，因而具有同等效果。由于最近推出的钆哌啶醇每毫摩尔钆具有更高的摩尔弛豫率，因此需要调整剂量（0.05 mmol/kg，而不是 0.1 mmol/kg bw 或 0.075 mmol/kg [钆布醇 CNS 检查]）。

图 29

颈动脉钆增强 MRI。

<!> 注意

非特异性细胞外 CA 的适应证

中枢神经系统

检测原发性肿瘤和脑转移、评估脱髓鞘疾病、检测感染和炎症过程、表征血管异常以及诊断大脑缺血和梗死。

腹部和盆腔

定位和定性病变，确定恶性肿瘤的扩散范围。

MR 血管造影

评估血管解剖结构和疾病。

乳腺

区分恶性和良性病变，检测多中心恶性肿瘤、复发性局部乳腺癌或良性治疗后纤维化。

肌肉骨骼系统

定位和定性肿块病变和炎症过程，以及评估疾病程度。

Blood Pool Agents

Blood pool agents are high molecular weight gadolinium compounds which have a slow diffusion rate from the intravascular into the extracellular space because of their albumin binding and which require metabolisation of their macromolecular moiety before renal excretion, so that **their concentration in plasma remains stable for over one hour**.

Blood pool agents* cause a significant reduction in the T1 relaxation time of circulating blood; thus, these agents are used for **MR angiography**, including coronary artery imaging, and for assessing tumour angiogenesis.

*) These blood pool agents are currently not available anymore.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

血池对比剂

血池对比剂是一种高分子量钆化合物，由于其与白蛋白结合，从血管内到细胞外空间的扩散速率较慢，并且在肾脏排泄前需要代谢其大分子部分，因此**其在血浆中的浓度可保持稳定一小时以上**。

血池对比剂* 可显著缩短循环血液的 T1 弛豫时间；因此，这些对比剂可用于 **MR 血管造影**（包括冠状动脉成像）以及评估肿瘤血管生成。

*) 这些血池对比剂目前已不再供应。

Organ-Specific Gadolinium-Based Contrast Agents

The two linear ionic complexes **Gd-BOPTA and Gd-EOB-DTPA** exhibit **liver specificity because of their selective uptake by hepatocytes and their partial hepatobiliary excretion.**

After intravenous administration, these CAs have an initial extracellular phase, which allows imaging of **hepatic vasculature**, followed by a **delayed hepatocytic uptake and biliary elimination phase**, which permits the evaluation of **hepatic tissue with altered functionality.**

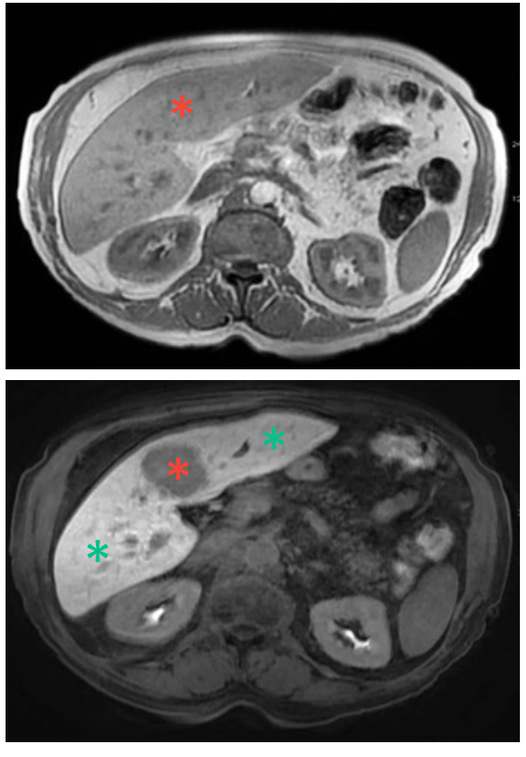

FIGURE 30

Liver MRI pre and 20 min post iv administration of Gd-EOB-DTPA with no uptake in an adenoma (red asterisk) and contrast agent uptake in normal liver tissue (green asterisk).

<!> ATTENTION

The uptake by hepatocytes selectively increases the signal intensity of normal liver parenchyma, while focal lesions containing mutated cells or altered structure do not uptake the CA and will appear hypointense, enhancing the visualisation of the lesion and helping to characterise its nature.

They can also be useful to improve detection of metastases and hepatocellular carcinoma.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

器官特异性含钆对比剂

两种线性离子型络合物 Gd-BOPTA 和 Gd-EOB-DTPA 具有肝脏特异性，这是由于其被肝细胞选择性摄取且部分通过肝胆系统排泄。

静脉注射后，这些 CA 首先经历细胞外分布期，可用于**肝血管成像**，随后进入**延迟性肝细胞摄取和胆汁排泄期**，可对功能改变的肝组织进行评估。

<!> 注意

肝细胞的摄取会选择性地增加正常肝实质的信号强度，而含有突变细胞或结构改变的局灶性病变不会摄取 CA，表现为低信号，这增强了病变的可视化并有助于突显其性质。

它们还有助于更好地检测转移灶和肝细胞癌。

图 30

Gd-EOB-DTPA IV 注射前和注射后 20 分钟的肝脏 MRI，腺瘤无摄取（红色星号），正常肝组织有对比剂摄取（绿色星号）。

Tissue Specific Reticuloendothelial and Lymph Node Agents

Superparamagnetic iron oxide particles (SPIO) are selectively taken up by the reticuloendothelial system (RES) through phagocytosis, with the size of the particles determining the tissue specificity.

Large SPIO are rapidly metabolised by phagocytic cells like Kupffer cells in the liver and spleen, producing negative contrast in T_2 weighted images. Since most liver lesions, including metastases and the vast majority of hepatocellular carcinomas, do not have an intact RES, their signal intensity is unchanged by administration of SPIO, so that the contrast between normal and abnormal liver tissue is increased as the lesion appears hyperintense relative to the normal tissue.

Large SPIO particles can be used in **liver and spleen imaging**.

Small SPIO with a core size under 10 nm enter the lymphatic system and are metabolised by phagocytes in normal lymph nodes, whereas metastatic lymph nodes retain a certain quantity of the CA, allowing to differentiate between normal tissue, which has a negative contrast enhancement in T_2 weighted images, and metastatic tissue, which maintaining high signal intensity.

Small SPIO particles are utilised in the study of **lymph nodes and bone marrow** (limited availability).

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

组织特异性网状内皮系统及淋巴结对比剂

超顺磁性氧化铁颗粒（Superparamagnetic iron oxide particles，SPIO）被网状内皮系统 (RES) 通过吞噬作用选择性摄取，其颗粒的大小决定了组织特异性。

大颗粒 SPIO 可被肝脏和脾脏中的 Kupffer 细胞等吞噬细胞迅速代谢，从而在 T_2 加权图像中产生阴性对比。由于大多数肝脏病灶（包括转移灶和绝大多数肝细胞癌）不具有完整的 RES，因此注射 SPIO 后其信号强度不会改变，正常肝组织与异常肝组织之间的对比度因此增强，表现为病灶相对于正常组织呈高信号。

大颗粒 SPIO 可用于**肝脏和脾脏成像**。

核心尺寸小于 10 nm 的**小颗粒 SPIO** 进入淋巴系统并由正常淋巴结中的吞噬细胞代谢，而转移淋巴结则保留一定量的 CA，这样就能区分在 T_2 加权图像中具有阴性对比增强的正常组织和保持高信号强度的转移组织。

小颗粒 SPIO 用于**淋巴结和骨髓研究**（可用性有限）。

Direct MR Arthrography

Direct MR arthrography involves the injection of a contrast agent into a joint region under fluoroscopic or ultrasound guidance, followed by magnetic resonance imaging. MR arthrography provides clearer images of the tendons, ligaments and cartilage in the affected region.

The low concentrated solutions correspond to 1:200-250 fold dilutions (2-2.5 mM) of the iv approved products (500-1000 mM).

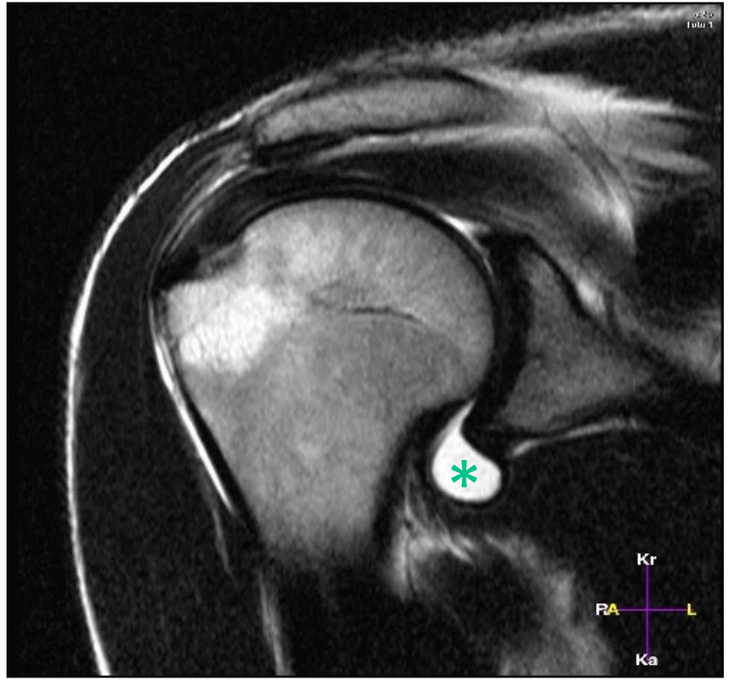

FIGURE 31

Direct MR arthrography of the shoulder using a 2.5 mM GBCA (Artirem®). GBCA in the joint space is indicated by an asterisk.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

直接磁共振关节造影术

直接磁共振关节造影术是指在透视或超声引导下将对比剂注入关节区域，然后进行磁共振成像。磁共振关节造影术可更清晰地显示受累区域的肌腱、韧带和软骨。

低浓度溶液相当于静脉给药获批产品 (500 mM～1000 mM) 的 1:200～250 倍稀释液 (2 mM～2.5 mM)。

图 31

使用 2.5 mM 含钆对比剂 (GBCA) (Artirem®) 进行肩关节直接磁共振关节造影。关节间隙内的 GBCA 用星号表示。

Dosage of Gadolinium Contrast Agents

For clinical use, the recommended dose of extracellular MR contrast agents is 0.1 mmol/kg of body weight for most of body imaging examinations. With the recent introduction of Gadopiclenol this agent can be used with 0.05 mmol/kg body-weight due to its higher molar relaxivity. When used in MR angiography and CNS imaging, some of the extracellular MR contrast agents may be utilised with a higher dose up to 0.3 mmol/kg body-weight (please refer to the SmPCs in your country).

Liver-specific contrast agents are effective in lower doses of 0.05 to 0.1 mmol/kg for Gadobenate (Gd-BOPTA) and 0.025 mmol/kg for Gadoxetate (Gd-EOB-DTPA).

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

钆对比剂的剂量

临床使用中，对于大多数人体成像检查，细胞外 MR 对比剂的推荐剂量为 0.1 mmol/公斤体重。最近推出的钆哌啶醇由于具有更高的摩尔弛豫率，因此可以使用 0.05 mmol/公斤体重的剂量。在 MR 血管造影和 CNS 成像中使用时，部分细胞外 MR 对比剂的剂量可提高至最高 0.3 mmol/公斤体重（请参考您所在国家的药品特性摘要 [SmPC]）。

肝脏特异性对比剂的有效剂量较低，钆贝酸 (Gd-BOPTA) 为 0.05～0.1 mmol/kg，钆塞酸 (Gd-EOB-DTPA) 为 0.025 mmol/kg。

/ Adverse Reactions

<!> ATTENTION

The most frequently reported adverse events of gadolinium contrast agents are rated as **mild** and include coldness, warmth or pain at the injection site, nausea, vomiting and headache, paresthesias and dizziness.

Allergic-like reactions with gadolinium complexes, which occur only **very rarely**, consist of sweating, rash, urticaria, itching and facial swelling.

Risk factors for developing an allergic-like reaction are a previous moderate or severe acute reaction to a gadolinium-based or iodinated contrast agent, asthma, and various other allergies.

Hypersensitivity is the major risk!

Pregnancy and lactation

In pregnant women, only when there is a very strong indication for an enhanced MRI, a macrocyclic gadolinium contrast agent may be administered using the smallest possible dose.

Breast feeding may be continued normally when macrocyclic gadolinium-based contrast agents are given to the mother.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 不良反应

<!> 注意

乳对比剂最常报告的不良事件等级为**轻度**，包括注射部位发冷、发热或疼痛、恶心、呕吐和头痛、感觉异常和头晕。

钆络合物**过敏样反应极少发生**，包括出汗、皮疹、荨麻疹、瘙痒和面部肿胀。

发生过敏样反应的风险因素是之前对含钆或含碘对比剂发生过中度或重度急性反应、哮喘以及各种其他过敏。

超敏反应是主要风险!

妊娠期与哺乳期

对于妊娠女性，仅在有强烈指征需要进行增强 MRI 检查时，才可使用最小可能剂量的大环类钆对比剂。

哺乳期女性使用大环类含钆对比剂后，可正常继续母乳喂养。

<!> ATTENTION

/ Nephrogenic Systemic Fibrosis (NSF)

Nephrogenic systemic fibrosis (NSF) is a rare but highly disabling disorder, which can occur in patients with highly impaired renal function exposed to less stable gadolinium-based CAs.

Clinical manifestations of NSF are extensive thickening and hardening of the skin and subcutaneous tissues associated with erythematous papules, as well as muscle weakness, bone pain and joint contractures.

Progressed NSF may also involve other organs, such as the liver, lungs, esophagus, heart and skeletal muscle.

Symptoms develop and progress rapidly, are irreversible and can lead to extreme disability and death because of scarring alterations of the organs with consequent loss of function.

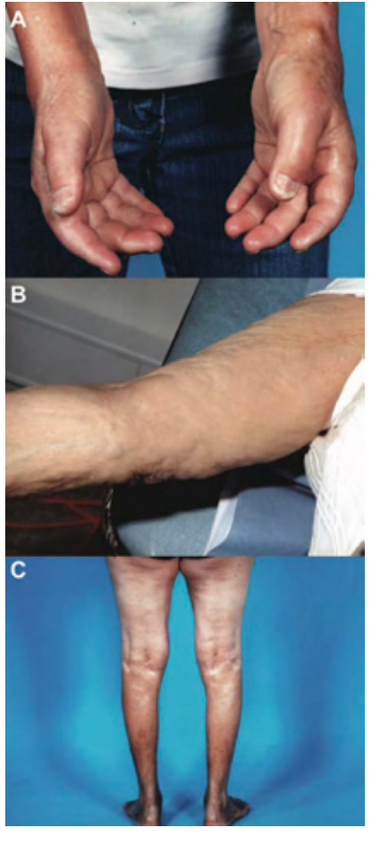

FIGURE 32

Manifestations of nephrogenic systemic fibrosis. **A**: Tightness and hardness of the hands combined with joint contractures. B: Firm nodules establishing a cobblestone configuration. **C**: Tight and firm skin on lower legs.

Reproduced from: Elmholdt TR et al., Nephrogenic Systemic Fibrosis in Denmark– A Nationwide Investigation. PLOS ONE 2013; 8(12): e82037. doi:10.1371/journal.pon e.0082037.0001

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

<!> 注意

/ 肾源性系统性纤维化 (NSF)

NSF 是一种罕见但高度致残的疾病，肾功能严重受损患者暴露于不太稳定的含钆对比剂时，会发生这种情况。

NSF 的临床表现为皮肤和皮下组织广泛增厚和硬化，伴有红斑状丘疹，以及肌肉无力、骨痛和关节挛缩。

进展型 NSF 还可能累及其他器官，如肝、肺、食管、心脏和骨骼肌。

症状发展和进展迅速，且不可逆，由于器官的瘢痕性改变及随之而来的功能丧失，可导致严重残疾甚至死亡。

图 32

肾源性系统性纤维化的表现。
A：手部紧绷、僵硬，并伴有关节挛缩。
B：形成鹅卵石样结构的坚硬结节。
C：小腿皮肤紧绷发硬。

来源：Elmholdt TR et al., Nephrogenic Systemic Fibrosis in Denmark– A Nationwide Investigation. PLOS ONE 2013; 8(12): e82037. doi:10.1371/iournal.pon e.0082037.0001

<!> ATTENTION

As a pathophysiological mechanism it is assumed that a reduced renal function, which is associated with a considerably prolonged tissue exposure to the gadolinium complex, increases the probability for precipitation of insoluble toxic gadolinium salts. This process is supposed to stimulate a subsequent proinflammatory cascade of events leading to the fibrosing process.

Risk Factors for the Development of NSF

The greatest risk factors for the development of NSF are a reduced renal function, particularly with a glomerular filtration rate of eGFR < 15 ml/min/1.73 m^2, and patients on dialysis.

The risk for developing NSF is substantially more pronounced after the administration of non-ionic and ionic linear gadolinium complexes, and it increases with contrast agent dose and multiple exposure.

Further risk factors include metabolic acidosis, elevated blood levels of iron, calcium or phosphate, a high-dose erythropoietin therapy, immunosuppression, vasculopathy and infection or other acute proinflammatory events.

Contrast Agents

对比剂

CHAPTER OUTLINE:

章节大纲：

<!> 注意

作为一种病理生理机制，认为肾功能下降（与钆络合物的组织暴露时间显著延长相关）增加了不溶性有毒钆盐沉淀的可能性。该过程被认为会激发后续的促炎级联反应，进而导致纤维化过程。

NSF 发生的风险因素

发生 NSF 的最大风险因素是肾功能下降（尤其是肾小球滤过率 eGFR < 15 mL/min/1.73 m^2 的患者）以及正在接受透析的患者。

使用非离子型和离子型线性钆络合物后发生 NSF 的风险明显更高，并且这种风险会随着对比剂剂量和多次暴露而增加。

其他风险因素包括代谢性酸中毒、血液中铁、钙或磷酸盐水平升高、高剂量促红细胞生成素治疗、免疫抑制、血管病变和感染或其他急性促炎事件。

/ Gadolinium Retention in the Brain

<!> ATTENTION

Repeated administration of gadolinium-based contrast agents is associated with gadolinium accumulation in the brain regions of the dentate nucleus and globus pallidus even in subjects with normal renal function.

While such deposits have been reported for all gadolinium-based agents, the highest levels found after the administration of **linear agents** were substantially higher than after the use of macrocyclic agents.

A significant positive correlation exists between the amount of gadolinium accumulated and the cumulative dose of previous administrations of gadolinium-based contrast agents.

To date, **no neurological symptoms associated with gadolinium retention in the brain** have been reported.

Gadolinium deposits may also occur in the **bone, liver and skin, independently of renal function**.

Bone and liver retention do not produce any clinical symptoms, whereas skin deposits manifest as red skin plaques.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 钆在大脑中的滞留

<!> 注意

即使在肾功能正常的个体中，**重复使用**含钆对比剂也会导致齿状核和苍白球脑区的钆蓄积。

虽然所有含钆对比剂均报告了此类沉积，但使用**线性对比剂**后的最高水平显著高于使用大环类对比剂后的水平。

钆蓄积量与既往使用的含钆对比剂累积剂量呈显著正相关。

迄今为止，**尚未报告与大脑中钆滞留相关的神经病学症状**。

钆沉积还可见于**骨骼、肝脏和皮肤，与肾功能无关**。

骨和肝潴留不会引起任何临床症状，而皮肤沉积表现为红色皮肤斑块。

/ Safety Recommendation

The **European Medicines Agency (EMA)** has classified the linear complexes Gd-DTPA-BMA, Gd-DTPA and Gd-DTPA-BMEA as high risk agents and suspended their intravenous usage, with the exception that Gd-DTPA may still be employed for direct MR arthrography.

The linear complexes Gd-BOPTA and Gd-EOB-DTPA, which are rated as intermediate risk agents, remain approved by EMA for hepato-biliary imaging only.

The macrocyclic agents are considered as low-risk and are maintained by EMA as non-specific gadolinium contrast agents. However, they should be used with caution in patients with GFR < 30 ml/min, observing a period of at least 7 days between two injections.

FIGURE 33

Image from Wikimedia Commons.
https://commons.wikimedia.org/wiki/File:Primum_Non_Nocere.jpg#filelinks

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 安全性建议

欧洲药品管理局（European Medicines Agency，EMA）将线性络合物 Gd-DTPA-BMA、Gd-DTPA 和 Gd-DTPA-BMEA 归类为高风险对比剂，并暂停其静脉注射使用，但 Gd-DTPA 仍可用于直接磁共振关节造影术。

线性络合物 Gd-BOPTA 和 Gd-EOB-DTPA 被 EMA 评定为中风险对比剂，目前仍仅获批用于肝胆成像。

大环类对比剂被视为低风险对比剂，EMA 将其保留为非特异性钆对比剂。但 GFR < 30 mL/min 的患者应谨慎使用，且两次注射之间至少间隔 7 天。

图 33

图片来自 Wikimedia Commons。
https://commons.wikimedia.org/wiki/File:Primum_Non_Nocere.jpg#filelinks

TYPE	IONICITY	PRODUCT	COMPLEX	EMA RECOMMENDATION
Linear	ionic	Gd-DTPA	gadopentetate dimeglumine	restricted use for direct MR arthrography
		Gd-BOPTA	gadobenate dimeglumine	restricted use as for hepato-biliary imaging
		Gd-EOB-DTPA	gadoxetate	restricted use as for hepato-biliary imaging
	non-ionic	Gd-DTPA-BMA	gadodiamide	suspended
		Gd-DTPA-BMEA	gadoversetamide	suspended
Macrocyclic	ionic	Gd-DOTA	gadoterate meglimine	maintained as non-specific GdCA
	non-ionic	Gd-HP-DO3A	gadoteridol	maintained as non-specific GdCA
		Gd-HP-DO3A	gadoteridol	maintained as non-specific GdCA
		Gadopiclenol	Gadopiclenol	approved 2023, non-specific

TABLE 4

Recommendation of the use of gadolinium-based CAs according to the European Medicines Agency (EMA). Since 2023 Gadopiclenol has been approved by EMA with the following characteristics: macrocyclic, non-ionic, non-specific GdCA

Contrast Agents

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章节大纲：

类型	离子性	产品	络合物	EMA 建议
线性	离子	Gd-DTPA	钆喷酸葡胺	限制用于直接磁共振关节造影术
		Gd-BOPTA	钆贝葡胺	限制用于肝胆成像
		Gd-EOB-DTPA	钆塞酸	限制用于肝胆成像
	非离子	Gd-DTPA-BMA	钆双胺	已暂停使用
		Gd-DTPA-BMEA	钆弗塞胺	已暂停使用
大环	离子	Gd-DOTA	钆特酸葡胺	保留为非特异性 GdCA
	非离子	Gd-HP-DO3A	钆特醇	保留为非特异性 GdCA
		Gd-HP-DO3A	钆特醇	保留为非特异性 GdCA
		钆哌啶醇	钆哌啶醇	2023 年获批，非特异性

表 4

欧洲药品管理局 (EMA) 关于含钆 CA 的使用建议。自 2023 年起，钆哌啶醇已获 EMA 批准，其特性如下：大环类、非离子型、非特异性含钆对比剂 (GdCA)

Ultrasound Contrast Agents

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

超声对比剂

/ Ultrasound Contrast Agents

Ultrasound contrast agents are used in order to **increase the reflection of ultrasound waves** from blood, thus resulting in an enhancement of the contrast between blood and surrounding tissue.

/ Microbubbles

Ultrasound contrast agents consist of suspensions containing microscopically small gas bubbles encapsulated in thin stabilising shells. The gas core of the microbubbles is generally composed of an inert high molecular weight and low solubility gas such as a perfluorocarbon or sulfur hexafluoride which does not diffuse across the shell and maintains an elevated vapour concentration within the microbubble. The stabilising shell is made of a biodegradable material, such as phospholipids or albumin, which reduces the likelihood of coalescence and allows the microbubbles to persist in the vasculature and permit diagnostic evaluation for several minutes.

/ 超声对比剂

使用超声对比剂是为了增加血液**对超声波的反射**，从而增强血液和周围组织之间的对比度。

/ 微泡

超声对比剂由混悬液组成，混悬液含有包裹在薄稳定壳层中的微小气泡。微泡的气体核心通常由惰性高分子量、低溶解度的气体（例如全氟化碳或六氟化硫）构成，其不会扩散穿过壳层，并能在微泡内维持较高的蒸气浓度。稳定壳层由磷脂或白蛋白等生物可降解材料制成，可降低凝聚的可能性，并使微泡在血管中持续存在，以便进行数分钟的诊断性评估。

Commercially available ultrasound contrast agents contain a **mixture of microbubbles of various sizes in the range of 1-10 µm, which is approximately the same size range as erythrocytes.** After intravenous injection the microbubbles **move passively with the blood** flow and act as tracers providing an enhanced ultrasound signal.

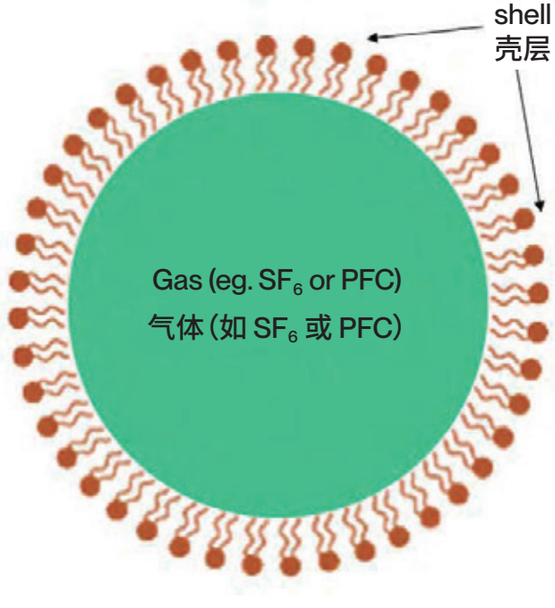


FIGURE 34

Structure of microbubble composed of a core of sulfur hexafluoride gas and a monolayer phospholipid shell.

>▪< FURTHER KNOWLEDGE

Composition of Currently Used Ultrasound Contrast Agents:

- Air microbubbles encapsulated in a shell of galactose stabilised with palmitic acid.
- Sulfur hexafluoride (SF_6) microbubbles encapsulated in a shell of phospholipids and palmitic acid.
- Perfluoropropane (perflutren, C_3F_8) microbubbles encapsulated in an albumin shell.
- Perfluoropropane (perflutren, C_3F_8) microbubbles encapsulated in a shell of phospholipids.

Contrast Agents

CHAPTER OUTLINE:

市售超声对比剂含有**1~10 µm 大小不等的微泡混合物，与红细胞的大小范围大致相同。**静脉注射后，微泡**随血流被动移动**并充当示踪剂，提供增强的超声信号。

图 34

微泡结构，由六氟化硫气体核心和单层磷脂壳组成。

>▪< 进阶知识

目前使用的超声对比剂的成分：

- 由棕榈酸稳定的半乳糖壳层包裹的空气微泡。
- 由磷脂和棕榈酸壳层包裹的六氟化硫 (SF_6) 微泡。
- 由白蛋白壳层包裹的全氟丙烷 (perflutren，C_3F_8) 微泡。
- 由磷脂壳层包裹的全氟丙烷 (perflutren，C_3F_8) 微泡。

对比剂

章节大纲：

/ Ultrasound Echo Enhancement by Microbubbles

The contrast enhancement achieved with microbubbles is due to a substantial difference in acoustic impedance at the interface between the microbubble structure and the surrounding blood plasma, which leads to backscattering of the sound wave at the microbubble surface.

This acoustic response of an ultrasound contrast agent is specific for the microbubbles used and also depends on the acoustic power of the irradiated ultrasound wave.

- at low acoustic powers, the microbubbles act as simple reflectors, so that only a backscattered linear signal can be received.
- at intermediate acoustic powers, the microbubbles are induced to oscillate and thereby to emit an intensive non-linear resonance signal, which contains, in addition to the fundamental vibration frequency, also harmonic upper frequencies.
- at even higher acoustic powers, the microbubble vibration is so violent that the microbubbles are destroyed by tearing of the membranes. This process is accompanied by emission of a detectable ultrasound pulse.

/ Contrast Agents

CHAPTER OUTLINE:

/ 微泡对超声回声的增强作用

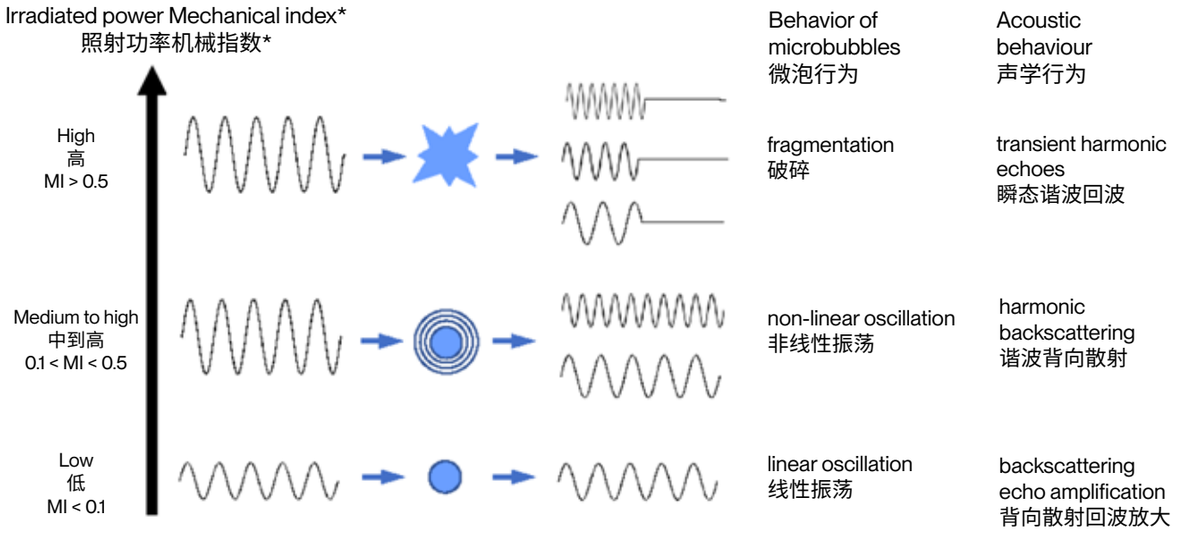
微泡实现的对比度增强效果源于微泡结构与周围血浆之间界面处声阻抗的显著差异，这导致声波在微泡表面发生反向散射。

超声对比剂的这种声学作用取决于所使用的微泡类型，同时也与所照射超声波的声功率相关。

- 在低声功率下，微泡充当简单的反射器，因此只能接收到反向散射的线性信号。
- 在中等声功率下，微泡被诱导振荡，从而发出强烈的非线性共振信号，该信号除了包含基频振动频率外，还包含谐波高频成分。
- 在更高的声功率下，微泡的振动变得非常剧烈，以至于微泡会因膜撕裂而被破坏。在此过程中会发出可检测到的超声脉冲。

/ 对比剂

章节大纲：



* The mechanical index (MI) is a unitless metric for the bioeffects of an ultrasound beam. It is proportional to the peak rarefaction pressure and inversely proportional to the frequency of the ultrasound wave.

FIGURE 35

Influence of irradiated ultrasound power on the acoustic behavior of microbubbles.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

* 机械指数（mechanical index，MI）是超声波束生物效应的无单位度量。它与峰值稀疏压力成正比，与超声波频率成反比。

图 35

照射超声功率对微泡声学行为的影响。

Implementation of contrast-specific ultrasound techniques such as harmonic and coded imaging and, particularly, phase and amplitude modulation, allows discrimination of the specific signal generated by the contrast agent microbubbles from other acoustic signals such as from specular reflection and tissue scattering.

The improved contrast effect permits real time scanning with the possibility of prolonged organ insonation, thus enabling dynamic imaging of blood flow and measuring organ perfusion with high sensitivity.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

实施对比剂特异性超声技术（如谐波成像和编码成像，尤其是相位调制和幅度调制技术），能够将对比剂微泡产生的特定信号与其他声学信号（如镜面反射和组织散射信号）区分开来。

增强的对比效果便于进行实时扫描，并可对器官进行长时间超声检查，从而能够对血流进行动态成像，并以高灵敏度测量器官灌注情况。

/ Biodistribution and Elimination

The intravascularly administered microbubbles are small enough to pass through the pulmonary capillaries and reach the systemic capillary network, but **they generally remain confined to the blood pool** and do not extravasate into the interstitial space.

However, some ultrasound contrast agents exhibit a postvascular hepato- and/or spleno-specific phase from 2 to 5 minutes after intravenous injection. This phenomenon is probably due to an adherence of the microbubbles to the hepatic sinusoids or to a selective uptake by the phagocytic Kupffer cells of the reticuloendothelial system.

After spontaneous dissolution of the microbubbles, the inert gas content is released and is mostly eliminated within 10 to 20 minutes by lung ventilation, whereas the shell material is metabolised and eliminated by the liver.

Ultrasound contrast agents are **not excreted** through the kidneys, and thus have no known nephrotoxicity.

No evidence of biological effects resulting from inertial cavitation – the rapid formation, growth and collapse of a gas cavity in a fluid as a result of intense ultrasound exposure – has been reported in humans.

/ Contrast Agents

CHAPTER OUTLINE:

/ 生物分布和消除

/ 对比剂

章节大纲：

血管内施用的微泡足够小，能够通过肺毛细血管并到达全身毛细血管网络，但**它们通常局限于血池内**，不会外渗到组织间隙。

然而，一些超声对比剂在静脉注射后 2 至 5 分钟会出现血管后肝和/或脾特异性显影期。这一现象可能是由于微泡黏附于肝窦，或被网状内皮系统的吞噬性 Kupffer 细胞选择性摄取所致。

微泡自发溶解后，惰性气体成分被释放，大部分在 10 至 20 分钟内通过肺通气排出，而壳层物质则通过肝脏代谢和消除。

超声对比剂**不经**肾脏排泄，因此无已知的肾毒性。

没有证据表明惯性空化（由于强烈的超声波暴露导致流体中气腔的快速形成、生长和塌缩）会对人类产生生物效应。

/ Administration of Ultrasound Contrast Agents

Ultrasound contrast agents are administered intravenously as a bolus injection or as a continuous infusion, or they are instilled into hollow structures, such as the urinary bladder.

Bolus injection produces a rapid rise in enhancement followed by a slower washout, and it is the most commonly used administration form for imaging with low and intermediate acoustic power.

Continuous infusion leads to a plateau-like enhancement and thus to a prolongation of the diagnostic time window that is important for quantifying tissue perfusion.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 超声对比剂的施用

超声对比剂可通过静脉推注或持续输注的方式给药，或被注入膀胱等中空器官内。

静脉推注可使增强效果迅速上升，随后缓慢廓清，是低至中等声功率成像最常用的给药方式。

持续输注可导致增强效果呈平台样，从而延长诊断时间窗，这对量化组织灌注很重要。

/ Indications

Ultrasound contrast agents are primarily used for **cardiovascular imaging**, including echocardiography, and for **ultrasound diagnostics of the liver and, less frequently, of other parenchymatous organs**.

Cardiovascular Imaging

In echocardiography, contrast agents are used for direct visualisation of the left ventricular chamber and endocardial surfaces, which permits clinical assessment of the left ventricular systolic function, structure and filling status. Ultrasound contrast agents are also applied for the examination of left ventricular structural abnormalities such as intracavitary thrombi, left ventricular aneurysms and pseudo aneurysms, the study of Takotsubo cardiomyopathy and myocardial perfusion.

Vascular Imaging

The clinical vascular applications using ultrasound contrast agents include contrast enhancement of the aorta, carotid arteries and the peripheral venous system. Specifically, ultrasound contrast agents are applied for examination of the carotid artery lumen and of atherosclerotic plaque neovascularisation, but also for the assessment of the intima-media-thickness as surrogate marker of systemic atherosclerosis.

/ 适应证

超声对比剂主要用于**心血管成像**（包括超声心动图），以及**肝脏超声诊断，较少用于其他实质器官的超声诊断**。

心血管成像

在超声心动图中，对比剂用于直接显示左心室腔和心内膜表面，可对左心室收缩功能、结构和充盈状态进行临床评估。超声对比剂还应用于检查左心室结构异常，如腔内血栓、左心室动脉瘤和假性动脉瘤、研究章鱼罐心肌病以及评估心肌灌注情况。

血管成像

超声对比剂在血管方面的临床应用包括主动脉、颈动脉和外周静脉系统的造影增强。具体来说，超声对比剂可用于检查颈动脉管腔和动脉粥样硬化斑块新生血管形成，也可用于评估作为全身动脉粥样硬化替代标志物的内膜中层厚度。

Liver Lesions

The main application area of contrast-enhanced ultrasound imaging is the **detection and characterisation of focal liver lesions, particularly the distinction between benign and malignant nodules**.

The differential diagnosis of hepatic tumours is facilitated by the highly sensitive visualisation of the capillary network achieved with ultrasound contrast media and the reliable information about tissue perfusion, which can be deduced from the influx and washout of the contrast agent.

After intravenous administration of the ultrasound contrast agent, three phases of enhancement in the liver can be distinguished:

- **the arterial phase**, in which the contrast agent reaches the liver first via the hepatic artery (up to 25s after injection)
- **the portal phase**, where the contrast agent has passed circulation and spreads through the liver in the portal branches (between 25 and 45s after injection)
- **the late or parenchymal phase**, in which the agent slowly distributes within the entire liver parenchyma (> 2 minutes after injection)

The characteristic features in these three phases allow detection of a hepatocellular carcinoma with high sensitivity and specificity, and they enable a differentiation of metastases in the liver.

肝脏病灶

对比增强超声成像的主要应用领域是**肝脏局灶性病变的定位和定性，尤其是良性和恶性结节的鉴别**。

超声对比剂可实现毛细血管网络的高灵敏度可视化，并且可从对比剂的流入和廓清中推断出关于组织灌注的可靠信息，这有利于肝肿瘤的鉴别诊断。

静脉注射超声对比剂后，肝脏的增强过程可分为三个时相：

- **动脉期**，对比剂首先通过肝动脉到达肝脏（注射后 25 秒内）
- **门静脉期**，对比剂进入循环并通过门静脉分支分布至肝脏（注射后 25～45 秒）
- **延迟期或实质期**，对比剂在整个肝实质内缓慢分布（注射后 > 2 分钟）

这三个时期的特征性表现有助于以高灵敏度和特异性检测肝细胞癌，并可对肝脏转移灶进行鉴别。

Further Indications

Other applications of ultrasound contrast agents include the detection and characterisation of breast, pancreatic, renal and endocrine tumours. Moreover, these agents are also used for the assessment of fallopian tube patency and of the vesico-ureteric reflux, but also for the identification of solid organ traumatic injury (**Fig. 36**).

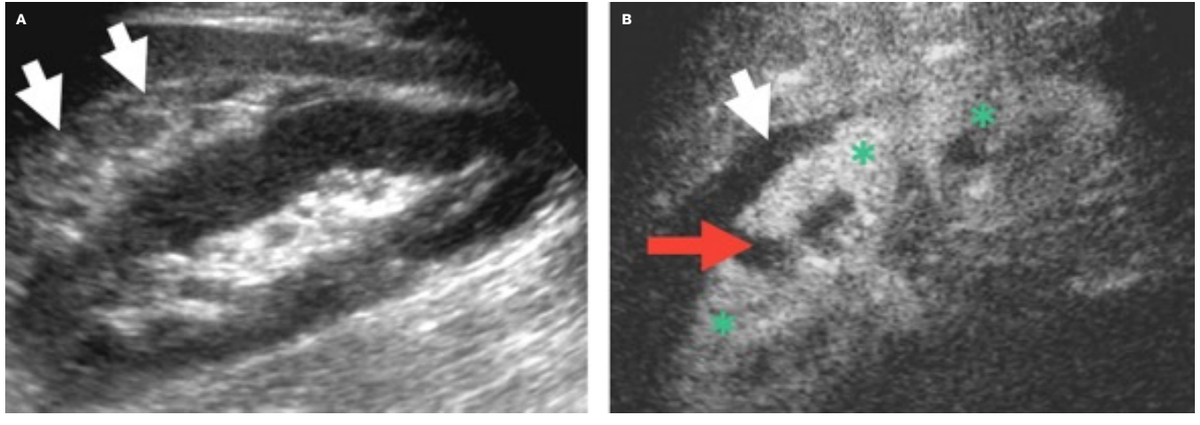


FIGURE 36

US images of the right kidney in a trauma patient before (A) and after (B) intravenous injection of a sonographic CA. On the image before CA administration (A), a heterogeneous peri-renal hematoma (white arrows) is seen, however, no kidney injury. The image after CA administration (B) shows in addition to the perirenal hematoma (white arrows) also a parenchymal laceration (red arrow). Note that following CA administration, the normal kidney parenchyma is strongly hyperechoic (asterisks). Images courtesy: Alexandra Platon, MD, University Hospitals Geneva.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

其他适应证

超声对比剂的其他应用包括乳腺、胰腺、肾脏和内分泌肿瘤的定位和定性。此外，这些对比剂还用于评估输卵管通畅性和膀胱输尿管反流，也可用于识别实体器官外伤性损伤（图 36）。

图 36

创伤患者静脉注射超声 CA 之前 (A) 和之后 (B) 的右肾超声影像。在注射 CA 前的图像 (A) 上，可见异质性肾周血肿（白色箭头），但无肾损伤。在注射 CA 后的图像 (B) 上，除肾周血肿（白色箭头）外，还显示肾实质裂伤（红色箭头）。需注意，注射 CA 后，正常肾实质呈强回声（星号）。图片来源：日内瓦大学医院 Alexandra Platon 医学博士。

/ Adverse Reactions

Adverse reactions associated with ultrasound contrast administration are **rare and usually of transient nature and mild intensity**.

The most common adverse events include tissue irritation at the site of injection, headache, nausea and vomiting, taste alterations, dyspnea, chest pain, hypo- or hypertension, vertigo, a sensation of warmth or flushing, cutaneous eruptions and asymptomatic premature ventricular contractions.

Hypersensitivity events are due to anaphylactoid reactions to the gas or shell and include hypotension, bronchospasm, urticaria and pruritus.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 不良反应

与使用超声对比剂相关的不良反应**较为罕见，通常为一过性且严重程度为轻度**。

最常见的不良事件包括注射部位组织刺激、头痛、恶心和呕吐、味觉改变、呼吸困难、胸痛、低血压或高血压、眩晕、温热感或潮红、皮疹和无症状室性期前收缩。

超敏反应事件是由于对气体或壳层的类过敏反应所致，包括低血压、支气管痉挛、荨麻疹和瘙痒。

Contraindications

Contraindications to intravenously administered microbubble contrast agents are a history of hypersensitivity reaction to the constituent gas or shell of the agents.

Due to the possible risk for a serious cardiopulmonary reaction, intravenous microbubble contrast agents should not be used in individuals with an **unstable cardiopulmonary condition** such as severe pulmonary hypertension, acute coronary syndrome, unstable angina, recent myocardial infarction, clinically unstable congestive heart failure and cardiac rhythm disorder.

Microbubble contrast agents should be avoided **in the 24 hours before extracorporeal shock wave treatment**.

Microbubble contrast agents should be used **in pregnancy only if the benefit outweighs the risk**. Breast feeding women may consider pumping and discarding of milk.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

禁忌证

静脉注射微泡对比剂的禁忌证是对对比剂组成气体或壳层有超敏反应史。

由于存在严重心肺反应的潜在风险，因此静脉内微泡对比剂不应用于患有**不稳定型心肺疾病**的个体，例如重度肺动脉高压、急性冠脉综合征、不稳定型心绞痛、近期心肌梗死、临床不稳定型充血性心力衰竭和心律失常。

体外冲击波治疗之前 24 小时内**应避免使用微泡对比剂**。

仅在获益大于风险时，方可在妊娠期使用微泡对比剂。哺乳期女性可考虑将乳汁抽出并丢弃。

/ Take-Home Messages

- / Contrast agents developed for radiographic examinations, magnetic resonance imaging and sonography have revolutionised the application field of diagnostic imaging in clinical practice.
- / Today's contrast agents are remarkably well tolerated and safe, but it remains the physician's responsibility to understand the potential adverse effects, and the specific situations, in which a particular patient might be at increased risk.
- / Radiographic contrast media (RCM) mainly comprise iodinated compounds that enhance image contrast by locally inducing a change in X-ray absorptivity.
- / Radiographic examinations using contrast media, which provide reliable diagnostic information regarding normal and abnormal morphology and function, are applied routinely in clinical practice for a plurality of indications.
- / The incidence of adverse reactions related to the intravascular administration of iodinated RCM, which has been drastically reduced with the change in usage from ionic high-osmolality RCM to nonionic low-osmolality or iso-osmolality RCM, is now generally low.
- / In patients with established hyperthyroidism, administration of iodinated RCM is contraindicated due to the risk for development of thyrotoxicosis.
- / Preexisting renal dysfunction is a significant risk factor for developing a contrast media-induced nephropathy.
- / MR contrast agents primarily comprise paramagnetic gadolinium complexes, which affect the relaxation times of water protons present in the surrounding tissue and thereby cause an increase or decrease in signal intensity.

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 核心要点

- / 为放射学检查、磁共振成像和超声检查开发的对比剂已彻底改变了诊断影像在临床实践中的应用领域。
- / 现今的对比剂具有良好的耐受性和安全性，但医生仍有责任了解潜在的不良反应以及特定情况下某些患者可能面临的风险。
- / 放射对比剂 (RCM) 主要包括碘化化合物组成，其通过局部改变 X 线吸收率的变化来增强图像对比度。
- / 使用对比剂进行的放射学检查，通过提供关于正常与异常形态和功能的可靠诊断信息，已在临床实践中广泛应用于多种适应证。
- / 与碘化 RCM 静脉注射相关的不良反应发生率，随着从离子型高渗透压对比剂转变为非离子型低渗透压或等渗透压对比剂的使用，已显著降低，现在普遍较低。
- / 确诊甲亢的患者禁用碘化 RCM，因其可能诱发甲状腺毒症。
- / 既往存在的肾功能不全是发生对比剂引起的肾病的重要风险因素。
- / MR 对比剂主要包括顺磁性钆络合物，其通过影响周围组织中水质子的弛豫时间，从而导致信号强度的增加或减少。

- Non-specific extracellular MR contrast agents are used for CNS and body imaging to asses pathologic processes and functional abnormalities, whereas organ and tissue specific contrast agents are used for detection and characterisation of tumours in liver, spleen, lymph nodes and bone marrow.
- Gadolinium-based MR contrast agents are well tolerated by the vast majority of patients, but the rate of adverse events tends to be higher with liver specific contrast agents than with extracellular gadolinium agents.
- Patients with impaired renal function may develop a nephrogenic systemic fibrosis after the administration of linear gadolinium complexes, which is why the European Medicines Agency (EMA) has suspended or restricted intravenous use of all high risk linear gadolinium-based contrast agents.
- Repeated administration of linear gadolinium-based contrast agents is associated with a dose-dependent accumulation of gadolinium in brain regions even in subjects with normal renal function.
- Ultrasound contrast agents consist of microbubbles composed of a high molecular weight and low solubility gas encapsulated in a stabilising shell, which backscatter the impinging ultrasound waves at their membrane due to a local change in acoustic impedance.
- Indications for ultrasound contrast agents primarily comprise cardiovascular imaging, including echocardiography, and the detection and charactersation of focal liver lesions, particularly the distinction between benign and malignant lesions.
- Ultrasound contrast agents benefit from an excellent safety profile, with the only, very rarely occurring adverse event being a hypersensitivity reaction.

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

- 非特异性细胞外 MR 对比剂用于中枢神经系统和全身影像学检查，以评估病理过程和功能异常，而器官和组织特异性对比剂则用于肝脏、脾脏、淋巴结和骨髓肿瘤的定位和定性。
- 绝大多数患者对含钆 MR 对比剂耐受良好，但肝脏特异性对比剂的不良事件发生率往往高于细胞外钆对比剂。
- 肾功能受损的患者在注射线性钆络合物后可能会发生肾源性系统性纤维化，这也是为什么欧洲药品管理局 (EMA) 已暂停或限制所有高风险线性钆基对比剂的静脉使用。
- 即使在肾功能正常的个体中，反复注射线性含钆对比剂也会导致钆在大脑区域的剂量依赖性蓄积。
- 超声对比剂由微泡组成，微泡内包裹着高分子量且溶解度低的气体，气体被稳定外壳包裹，由于声阻抗的局部变化，微泡会在其膜层对入射的超声波产生背向散射。
- 超声对比剂的适应证主要包括心血管成像（如超声心动图）以及肝脏局灶性病变的定位和定性，特别是良性与恶性病变的区分。
- 超声对比剂具有极佳的安全性，其唯一且非常罕见的不良反应是过敏反应。

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Contrast Agents

CHAPTER OUTLINE:

对比剂

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Test Your Knowledge

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

知识测试

Test Your Knowledge

<?> QUESTION

1 Which elements are incorporated in routinely used RCM?

- ☐ Manganese in form of superparamagnetic particles
- ☐ Iodine in form of organic molecules
- ☐ Barium as barium sulfate suspension
- ☐ Gadolinium in form of chelating complexes
- ☐ Xenon as gas

Contrast Agents

CHAPTER OUTLINE:

对比剂

章节大纲：

知识测试

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1 常规使用的 RCM 中包含哪些元素？

- ☐ 锰以超顺磁性粒子形式存在
- ☐ 碘以有机分子形式存在
- ☐ 硫酸钡作为硫酸钡悬浮液
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/ Test Your Knowledge

<?> QUESTION

2 Which of the following statements regarding iodinated RCM are correct?

- ☐ RCM with a carboxylate substituent dissociate in solution forming ionic compounds
- ☐ Highly hydrophilic RCM have an enhanced plasma protein binding
- ☐ Iodinated RCM in solution undergo a deiodination process releasing free iodide
- ☐ A cholegraphic RCM has an accelerated glomerular filtration rate
- ☐ Osmolality is higher in ionic RCM than in non-ionic RCM, each with the monomeric agents having a higher osmolality

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

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2 关于碘化 RCM，下列哪些说法是正确的？

- ☐ 含有羧酸盐取代基的 RCM 在溶液中解离形成离子化合物
- ☐ 高亲水性 RCM 的血浆蛋白结合力增强
- ☐ 溶液中的碘化 RCM 经过脱碘过程，释放游离碘离子
- ☐ 胆道对比剂 (cholegraphic RCM) 具有加速肾小球滤过率的特性。
- ☐ 离子型 RCM 的渗透压高于非离子型 RCM，且单体型对比剂的渗透压更高

/ Test Your Knowledge

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/ 对比剂

章节大纲：

Test Your Knowledge

<?> QUESTION

3 Which factors are associated with an increased risk for adverse effects using RCM?

- ☐ Radiographic imaging of the gastrointestinal tract using barium sulfate suspension
- ☐ Intravenous administration of high osmolality RCM
- ☐ Intravenous cholangiographic contrast media to patients with an undelaying thyroid disorder
- ☐ Intravenous administration of high viscosity RCM
- ☐ Visualisation of the gastrointestinal tract with oral iodinated RCM

Contrast Agents

CHAPTER OUTLINE:

知识测试

对比剂

章节大纲：

<?> 问题

3 哪些因素与使用 RCM 时发生不良反应风险增加相关?

- ☐ 使用硫酸钡混悬液进行胃肠造影
- ☐ 静脉注射高渗透压 RCM
- ☐ 向甲状腺疾病患者静脉注射胆道对比剂
- ☐ 静脉注射高粘度 RCM
- ☐ 口服碘化 RCM 进行胃肠道成像

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对比剂

章节大纲:

Test Your Knowledge

<?> QUESTION

4 Which patients are at risk for developing post-contrast acute kidney injury after administration of iodinated RCM?

- ☐ Patients with impaired renal function with eGFR < 45 ml/min/1.73 m^2
- ☐ Patients suffering from multiple myeloma
- ☐ Patients suffering from diabetes mellitus
- ☐ Patients suffering from cardiovascular disease

Contrast Agents

CHAPTER OUTLINE:

知识测试

对比剂

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- ■ 糖尿病患者
- ■ 心血管疾病患者

Test Your Knowledge

<?> QUESTION

5 Which compounds are routinely used as MR contrast agents?

- ☐ Gd^{3+} in form of complexes with chelating ligands
- ☐ Perfluorocarbon nanoparticles for ^{19}F imaging
- ☐ Fe_2O_3 nanoparticles
- ☐ Mn^{2+} in form of complexes with chelating ligands

Contrast Agents

CHAPTER OUTLINE:

知识测试

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5 哪些化合物是常用的 MR 对比剂?

- ☐ 与螯合配体形成络合物形式的 Gd^{3+}
- ☐ 用于 ^{19}F 成像的全氟化碳纳米颗粒
- ☐ Fe_2O_3 纳米粒子
- ☐ 与螯合配体形成络合物形式的 Mn^{2+}

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- ■ 与螯合配体形成络合物形式的 Mn^{2+}

对比剂

章节大纲:

/ Test Your Knowledge

<?> QUESTION

6 Which statements about non-specific extracellular contrast agents are correct?

- ☐ They circulate freely in the extracellular space but do not penetrate the intact blood-brain barrier
- ☐ They require metabolisation of their macromolecular moiety before renal excretion
- ☐ They are applied for CNS examinations
- ☐ The various extracellular gadolinium contrast agents show widely varying efficiencies with respect to their relaxivity

/ Contrast Agents

CHAPTER OUTLINE:

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章节大纲：

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- ☐ 它们在细胞外空间自由循环，但不能穿透完整的血脑屏障。
- ☐ 在经肾脏排泄前，其大分子部分需要代谢
- ☐ 它们用于 CNS 检查
- ☐ 各种细胞外钆对比剂的弛豫效能差异很大

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- [x] 它们用于 CNS 检查
- [ ] 各种细胞外钆对比剂的弛豫效能差异很大

/ Test Your Knowledge

<?> QUESTION

7 Which MR contrast agents are recommended for detection and characterisation of liver tumours?

- ☐ Linear ionic Gd^{3+} complexes
- ☐ Linear non-ionic Gd^{3+} complexes
- ☐ Macrocyclic Gd^{3+} complexes
- ☐ Large superparamagnetic iron oxide particles
- ☐ Small superparamagnetic iron oxide particles

CHAPTER OUTLINE:

章节大纲：

/ 知识测试

<?> 问题

7 推荐用于定位和定性肝脏肿瘤的 MR 对比剂有哪些？

- ☐ 线性离子 Gd^{3+} 络合物
- ☐ 线性非离子 Gd^{3+} 络合物
- ☐ 大环类 Gd^{3+} 络合物
- ☐ 超顺磁性氧化铁大颗粒
- ☐ 超顺磁性氧化铁小颗粒

/ Test Your Knowledge

<?> ANSWER

7 Which MR contrast agents are recommended for detection and characterisation of liver tumours?

- [x] Linear ionic Gd^{3+} complexes
- [ ] Linear non-ionic Gd^{3+} complexes
- [ ] Macrocyclic Gd^{3+} complexes
- [x] Large superparamagnetic iron oxide particles
- [ ] Small superparamagnetic iron oxide particles

CHAPTER OUTLINE:

章节大纲：

/ 知识测试

<?> 回答

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/ Test Your Knowledge

<?> QUESTION

8 Which of the following are risk factors for developing a nephrogenic systemic fibrosis after administration of a gadolinium-based contrast agent?

- ☐ Impaired renal function with a glomerular filtration rate of eGFR < 15 ml/min/1.73 m^2
- ☐ Patients suffering from a hepatic disease
- ☐ Administration of a linear gadolinium contrast agent
- ☐ Patients with elevated blood levels of iron
- ☐ Application of superparamagnetic iron oxide particles

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

<?> 问题

8 下列哪些是使用含钆对比剂后发生肾源性系统性纤维化的危险因素？

- ☐ 肾功能损害，肾小球滤过率 eGFR < 15 mL/min/1.73 m^2
- ☐ 肝病患者
- ☐ 注射线性钆对比剂
- ☐ 高铁血症患者
- ☐ 应用超顺磁性氧化铁颗粒

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章节大纲：

/ Test Your Knowledge

<?> QUESTION

9 What are the recommendations of the European Medicines Agency (EMA) about the use of gadolinium-based CAs regarding the risk of developing nephrogenic systemic fibrosis?

- ☐ The use of all linear gadolinium-based complexes is suspended
- ☐ The use of macrocyclic ionic gadolinium-based complexes is restricted to hepato-biliary imaging
- ☐ The use of linear non-ionic gadolinium-based complexes is suspended
- ☐ The use of linear ionic gadolinium-based complexes is restricted to hepato-biliary imaging and arthrography, respectively

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

<?> 问题

9 欧洲药品管理局 (EMA) 针对使用钆基对比剂引发肾源性系统性纤维化风险的建议是什么？

- ☐ 暂停使用所有线性含钆络合物
- ☐ 大环类离子型含钆络合物仅限用于肝胆成像
- ☐ 暂停使用线性非离子型含钆络合物
- ☐ 线性离子型含钆络合物的使用分别仅限用于肝胆成像和关节造影

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/ Test Your Knowledge

<?> QUESTION

10 Which statements regarding the use of microbubbles as ultrasound contrast agents are correct?

- ☐ They are excreted through the kidneys
- ☐ They are mostly eliminated through the lung
- ☐ They cannot be used for measuring the tissue perfusion of the liver
- ☐ They can rapidly pass an intact blood-brain barrier
- ☐ They generally remain confined to the blood pool

CHAPTER OUTLINE:

/ 知识测试

<?> 问题

10 关于使用微泡作为超声对比剂，下列哪些说法是正确的？

- ☐ 通过肾脏排泄
- ☐ 大多通过肺消除
- ☐ 不能用于测量肝脏的组织灌注
- ☐ 可以快速通过完整的血脑屏障
- ☐ 通常局限于血池内

章节大纲：

/ Test Your Knowledge

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章节大纲：

/ Test Your Knowledge

<?> QUESTION

11 What are the advantages of ultrasound imaging using microbubble contrast agents?

- ☐ They allow real time imaging of blood flow and organ perfusion with high sensitivity
- ☐ The microbubbles can also be therapeutically used for targeted drug delivery
- ☐ They have an excellent safety profile
- ☐ The new generation microbubbles with improved stability can persist under insonation with high acoustic power

/ 知识测试

<?> 问题

11 使用微泡对比剂进行超声成像的优势有哪些?

- ☐ 以高灵敏度实时成像对血流和器官灌注情况
- ☐ 微泡还可用于靶向给药治疗
- ☐ 它们具有极佳的安全性
- ☐ 新一代微泡具有更高的稳定性，可在高声功率超声照射下持续存在

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/ Test Your Knowledge

<?> QUESTION

12 Which imaging method is indicated for the detection of a hepatocellular carcinoma in a patient with renal insufficiency?

- ☐ Radiographic imaging using iodinated RCM
- ☐ Ultrasound imaging using microbubbles contrast agents
- ☐ MR imaging using the liver-specific linear gadolinium complexes

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

<?> 问题

12 肾功能不全患者检测肝细胞癌，应选择哪种影像学方法?

- ☐ 使用碘对比剂进行放射学成像
- ☐ 使用微泡对比剂进行超声成像
- ☐ 使用肝脏特异性线性钆络合物的 MR 成像

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/ Test Your Knowledge

<?> QUESTION

13 Which functional principles determine liver specificity in the different imaging methods?

- ☐ Partial distribution of contrast agent in the liver through passive diffusion, used in radiographic examinations
- ☐ Selective uptake of contrast agent by phagocytic cells in the liver, used in MR imaging
- ☐ Partial hepatobiliary excretion and uptake of contrast agent by hepatocytes, used in MR imaging
- ☐ Accumulation of contrast media depending on the functionality of the hepatobiliary system, used in ultrasound imaging

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

<?> 问题

13 不同成像方法中决定肝脏特异性的功能原理有哪些？

- ☐ 放射影像学检查中，通过被动扩散使对比剂在肝脏中分布
- ☐ 对比剂被肝脏中的吞噬细胞选择性摄取的特性应用于 MR 成像中
- ☐ 对比剂部分经肝胆排泄和肝细胞摄取的特性应用于 MR 成像中
- ☐ 对比剂积聚程度取决于肝胆系统功能情况的特性应用于超声成像中

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/ Test Your Knowledge

<?> QUESTION

14 Which statements concerning adverse reactions in respect of the various imaging methods are correct?

- ☐ The incidence of adverse reactions related to iodinated RCM has been reduced in routine clinical practice due to the restricted use of ionic high-osmolality RCM
- ☐ Orally administered iodinated contrast media for radiographic imaging of the gastrointestinal tract are contraindicated in patients with suspected perforation
- ☐ Repeated administration of linear gadolinium-based contrast agents is associated with a dose-dependent accumulation of gadolinium in brain regions even in subjects with normal renal function.
- ☐ Microbubble ultrasound contrast agents increase the risk for pulmonary embolism
- ☐ In patients with established hyperthyroidism, administration of iodinated contrast media is contraindicated

/ Contrast Agents

CHAPTER OUTLINE:

/ 对比剂

章节大纲：

/ 知识测试

<?> 问题

14 关于各种成像方法的不良反应，下列哪些说法是正确的？

- ☐ 由于离子型高渗对比剂的限制使用，临床实践中碘化相关不良反应的发生率已有所降低
- ☐ 对疑似消化道穿孔患者禁用口服碘化对比剂进行胃肠道影像学检查
- ☐ 即使在肾功能正常的个体中，反复注射线性含钆对比剂也会导致钆在大脑区域的剂量依赖性蓄积。
- ☐ 微泡超声对比剂会增加肺栓塞的风险
- ☐ 对于已确诊的甲状腺功能亢进患者，禁用含碘对比剂

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