INTRODUCTION

Historical Aspects

The field of radiography including the development of contrast media for this diagnostic tool is based on the discovery of X-rays by the physicist Wilhelm Conrad Röntgen. Later on, the rays he discovered came to be called “Roentgen rays” in his honor.

Experimenting with electrons Röntgen observed effects he attributed to so-called cathode rays, hitherto unknown rays, which he called “X-rays”. To prove his ideas and the penetration of different kinds of matter by this new type of radiation, Röntgen used a fluoroscope and a photographic plate. On December 22, 1895, he succeeded in taking a picture of the bones of his wife’s hand using X-rays.

Röntgen assumed his newly discovered rays to be electromagnetic radiation like visible light. In April 1912, this assumption was confirmed by the physicist Max von Laue and his coworkers. The wave-like behavior of X-rays was proven by the detection of diffraction and interference patterns produced by X-rays transmitted through crystals.

Physicians all over the world soon recognized the diagnostic potential of Röntgen’s discovery. The new rays gave physicians the ability to see inside the body and obtain pictures not only of bones and soft tissues but also of hollow organs by using radiopaque substances. In 1896, barium sulfate (BaSO4) was used for the first time to examine intestinal peristalsis, a procedure which was soon to fall into oblivion again. Only ten years later, the so-called Rieder meal (barium mixed with gruel) was introduced for X-ray examinations of the gastrointestinal tract.

U. Speck, *X-Ray Contrast Media*, https://doi.org/10.1007/978-3-662-56465-3_1

While the ability of iodine to absorb X-rays was discovered as early as 1896, it took almost another thirty years to develop the first X-ray contrast medium (XCM) for clinical use. The oily iodine compound Lipiodol was introduced as the first reliable X-ray contrast agent for myelography. In 1924, the first oral biliary XCM, Iodtetragnost (iodophthalein) for visualization of the gallbladder was put on the market. This was followed by the introduction of less toxic cholecystographic XCM like Biliselectan (iodoalphionic acid) in 1940 and later on the more tolerable Biloptin (sodium iopodate). In 1953, Biligrafin (adipiodone) was established as the first i.v. XCM for visualizing the gallbladder and biliary tract in the routine diagnostic setting. Further development led to another two well-tolerable XCM − Endomirabil (iodoxamic acid) and Biliscopin (iotroxic acid) − agents that are mostly used in cholecystocholoangiography.

Uroselectan was the first reliable urographic contrast agent. It is a water-soluble organic iodine compound that is excreted via the kidneys and entered the market in 1929. Concomitantly, the long line of soluble XCM with iodinated pyridine rings and later on with benzene rings began.

In the early 1950s, there was a rapid switch from diiodinated pyridine derivates to benzene derivates with three iodine atoms, the tri-ioidinated benzoic acid.

Hydrophilic side groups as well as methylglucamine, which is used for salt formation, significantly improved the tolerance of ionic XCM.

In the late 1960s, the significance of hyperosmolality but also that of electric charge as causes of specific adverse effects of ionic XCM became clear. Almen's suggestion to replace the ionic carboxyl group in tri-iodinated benzoic acid derivates with a non dissociated group, i.e. a carbohydrate, and to ensure the necessary water solubility by utilizing particularly hydrophilic hydroxyl groups marks the beginning of nonionic XCM. The latest advancement of X-ray contrast agents led to the hexa-iodinated, nonionic dimers Iotrolan and Iodixanol, which have the same osmolality as blood and cerebrospinal fluid at all concentrations.

The initial expectation that iso-osmolality would further improve the side effect profile has not been confirmed in clinical studies. Therefore, the tri-iodinated monomeric nonionic contrast media remain the workhorse in contrast-enhanced X-ray examinations.

Nonionic monomeric or dimeric X-ray contrast media are applied in all areas of diagnostic radiology.

In addition to the positive XCM mentioned so far, negative XCM such as air, oxygen and carbon dioxide, which absorb X-rays less well than biological tissues, are applied for visualizing hollow organs. The use of negative XCM has become rare with the advent of sophisticated imaging modalities such as CT and MRI.

Contrast media in X-ray imaging

The significance of contrast media was recognized almost simultaneously with the discovery of X-rays. Too many structures in the body remain invisible when X-rays alone are used and can only be made visible after administration of a contrast medium.

As a result, much effort has been spent to better adapt contrast agents and the techniques of their administration to diagnostic requirements and to improve their tolerability.

At the same time, imaging technologies have continued to develop, and computed tomography and subtraction techniques improve the contrast resolution of X-ray images. However, contrast media still have their uses with new imaging modalities as well.

Visualization of functions

- elimination (kidney, liver)
- transport processes (bloodstream, cerebrospinal fluid, intestinal contents, imaging of the liver)
- perfusion (all organs)
- permeability and barriers (blood-brain barrier, cysts)

Morphology

- Creating and increasing contrasts, for example, through
  - varying contrast media concentrations in individual tissues
  - temporal changes of radiation absorption or signal intensities

On the whole, all imaging techniques and all products referred to as contrast media have one thing in common − they all assist in providing visual representations of information from within the body.

This information may represent anatomical structures, functions, or physical-chemical conditions.