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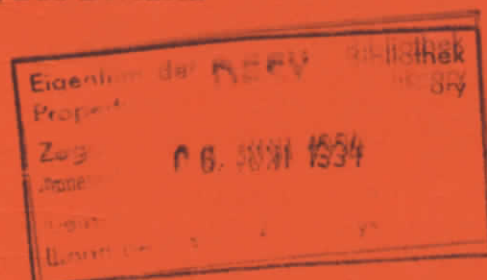
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Coronary angiography with synchrotron radiation

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Abstract

Worldwide several systems for Digital Subtraction Angiography in energy subtraction mode (dichromography) are developed. One of the systems which allows investigations of patients - the system NIKOS in the Hamburger Synchrotronstrahlungslabor HASYLAB at DESY is described. The system consists out of six main parts: The 20 pole wiggler HARWI in the beamline W2 of the storage ring DORIS, the two beam monochromator for the two 12.5 cm wide monochromatic X-ray beams, the safety system, the fast scanning device, the fast low-noise two-line ionization chamber and the computer system.

Since 1990 patients were investigated with the system NIKOS. Aim of the work is to visualize coronary arteries down to 1 mm diameter with an iodine mass density of 1 mg/cm², thus allowing non-invasive investigations by intravenous application of the contrast medium. The two images for subtraction are simultaneously taken with photon energies just below and above the iodine K-edge (33.17 keV) in a line scan mode.

Intravenous angiograms from investigations with version III of the system NIKOS are presented and the next steps for getting an increased image quality are described.

1. Introduction

Today in most of the synchrotron radiation facilities worldwide systems for medical applications like multiple energy computed tomography, micro beam radiation therapy, mammography and intravenous coronary angiography are under development. The most advanced application of synchrotron radiation for medical purposes is intravenous coronary angiography on the base of digital subtraction angiography (DSA) in energy subtraction mode (dichromography). Systems for dichromography are under development at the NSLS in Brookhaven, USA⁽¹⁾ (before at SSRL in Stanford, USA⁽²⁾), at VEPP in Novosibirsk, Russia⁽³⁾, at HASYLAB in Hamburg, Germany⁽⁴⁾, at the Photon Factory in Tsukuba, Japan^(5,6) and at the ESRF in Grenoble, France⁽⁷⁾. Only two of these systems - the system at the NSLS and the system NIKOS at HASYLAB - currently allow the investigation of patients. Both are line scan systems. the setups are very similar in principle, and the quality of the resulting images is comparable. Therefore, in this paper only the system NIKOS is described in detail. The system NIKOS is installed in the beamline W2 of the storage ring DORIS at the Hamburger Synchrotronstrahlungslabor HASYLAB at DESY in Hamburg.

Dichromography eliminates the need for arterial catheterization of the coronary arteries thus diminishing the risks to the patient. The aim of the work is to visualize coronary arteries as small as 1 mm in diameter with an iodine mass density of 1 mg/cm². following intravenous injection of the contrast agent. In conventional DSA, normally used for intravenous investigations, the images with different iodine contrast are taken at different times. This time subtraction mode is not suitable for the imaging of small coronary arteries because of the fast motion of the heart. For the dichromography the two images for subtraction are simultaneously taken with photon energies just below and above the iodine K-edge (33.17 keV). This results in two images with different iodine contrast and almost no differences for bone and soft tissue. The method is 10000 times more sensitive to iodine than to soft tissue what allows the imaging of structures with very low mass density of iodine.

The system NIKOS was developed since 1981. In 1990 human studies began. The quality of the first images was not suited for clinical routine evaluations. Meanwhile a remarkable increase of image quality was achieved especially since the installation of version III of the system NIKOS mid of 1993. This version of the system is described in section 2. Examples of the images are given in section 3 followed by an outlook in section 4.

2. The NIKOS III system

Because NIKOS is a line scan system the background signals from scattered radiation are reduced remarkably. The system performance parameters for intravenous contrast medium injections within 250 ms, in a field of 12.5×12.5 cm², are given in ref. (8). The version III of the NIKOS system consists out of six main components (Fig.1).

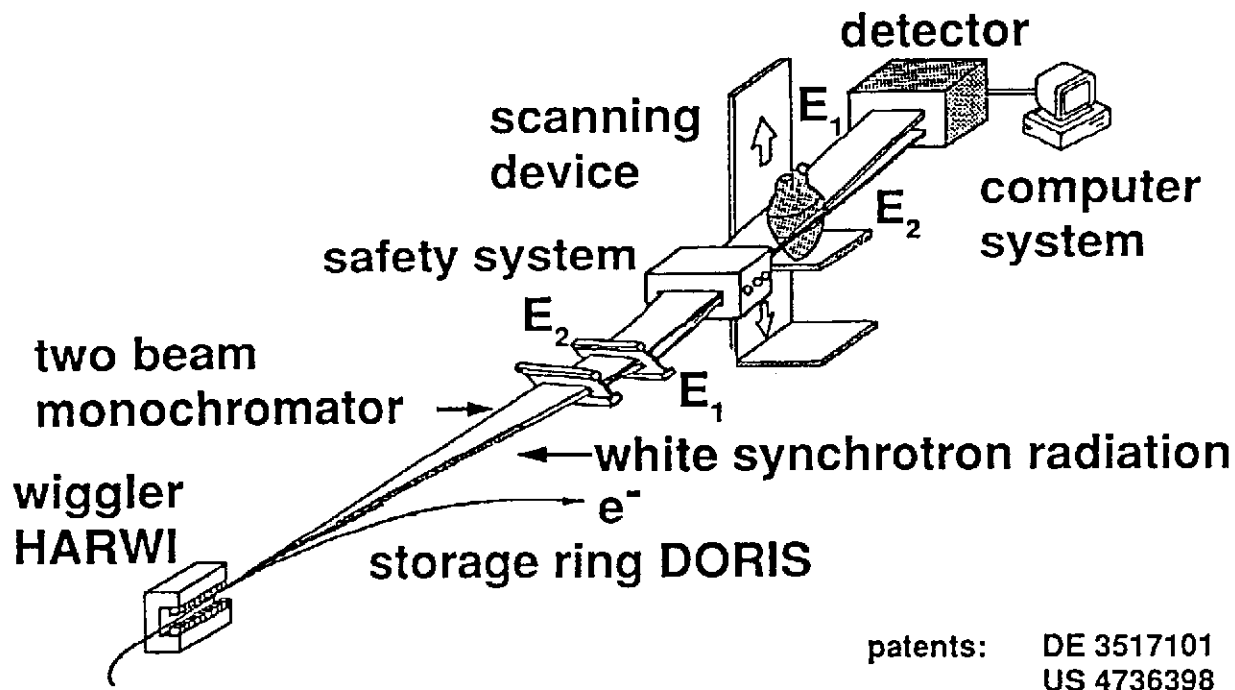


Figure 1: Scheme of the experimental setup

- The 20 pole wiggler HARWI⁽⁹⁾ has a length of 2.4 m plus 0.12 m for the endpoles. After installation of a variable vacuum chamber the minimal magnetic gap is 30 mm high and the maximum field strength amounts to 1.26 T. During the investigation of the patients DORIS operated at an energy of 4.5 GeV (2 or 5 bunches), with a current of about 50 mA. For these conditions the critical energy is 17.0 keV and the horizontal opening angle is 6.4 mrad.
- The two monochromatic X-ray beams are diffracted out of the white synchrotron radiation beam by the monochromator. A 0.6 mm thick, 11 mm high and 112 mm wide Si(111) crystal is installed in Laue geometry for each monochromatic beam. Following an idea in ref. (10) the crystals are bent with a radius of 11 m in order to focus the beam thus increasing the flux at the patient. The fluence was measured to be $0.8 \cdot 10^{11}$ photons/(mm²·s) for 50 mA current in DORIS. This is an increase of a factor 6 compared to the former monochromator with two Ge(111) crystals in Bragg geometry. The crystals are cut asymmetrically (asymmetry angle 35.26°). They are installed in a He-filled tube and cooled by water. The height of the beams is 1.7 mm at the monochromator, 0.6 mm at the patient and 0.9 mm at the detector. The bandwidth of the monochromatic beams is 180 eV, the energy separation 300 eV.
- A redundant safety system with three independent shutters switches off the monochromatic beams within less than 10 ms in case of any system failure.
- The fast scanning device can move loads of up to 300 kg over a distance of 20 cm with constant speed up to 50 cm/s (precision 1%). During the human study runs the scanning device ran with 12 cm/s to 23 cm/s. Its moving force is generated by

a hydraulic system. It is equipped with a chair for the patient. The chair allows for a patient rotation of $\pm 180^\circ$ about the vertical axis and $\pm 20^\circ$ about the lateral axis in order to set the appropriate projection angles. During the vertical scan of the patient a precise optical scale triggers the readout of the detector every 0.5 mm (August 1993) or 0.4 mm (November 1993), respectively. Thus the vertical pixel size in the images is defined.

- As a detector a fast low-noise two-line ionization chamber⁽¹¹⁾ is installed which simultaneously records the two lines with the energy above and below the K-edge, respectively. It has a common drift cathode and for each line a Frisch grid and 256 Cu-strips as anodes. The 17 μm thick and 55 mm long Cu-strips are directed along the monochromatic beams. The center-to-center distance of the strips is 0.4 mm thus defining the horizontal pixel size in the images. The chamber is filled with 90% of Kr gas and 10% of CO₂ under 14 bar pressure. The 0.5 mm thick entrance window is made of carbon fiber imbedded in polyimide matrix. In front of it a collimator with two slits of 1.8 mm vertical height each and a center-to-center distance of 2.8 mm is mounted.

The ionization current of each strip is summed up in resettable integrators whose output is transferred in parallel into sample-and-hold registers and afterwards digitized with one 16-bit ADC (Analogic DVX 2503) per line. The readout time per line is 2 ms. The data are transmitted to the computer via two glass fiber links with a maximal transfer rate of 4.4 Mbaud.

The dynamic range of the complete detector system was measured to be 40000:1. The detective quantum efficiency of the complete system

$$\text{DQE} = \frac{(\text{SNR}_{OUT})^2}{(\text{SNR}_{IN})^2}$$

(SNR_{OUT} = signal-noise-ratio in the images, SNR_{IN} = signal-noise-ratio in front of the detector; $(\text{SNR}_{IN})^2 = N_\gamma$ = number of photons per pixel) was determined to be $\text{DQE} = 58\%$ for 33 keV photons.

- The computer system consists of a VAX station 3500 for the coordination of the computer system, for data acquisition, image processing and presentation and a PDP 11/73 for control of the system. The two machines are linked via a serial line and connected to the DESY computer center (IBM ES 9000/720 VF). In the center the data are stored in a data base (DB2).

3. Results of human studies

During 1993 after installation of the NIKOS III system seven patients were studied in two different periods. Each investigation started with a positioning run with reduced skin dose (15 mGy in a field of $10.1 \times 12.8 \text{ cm}^2$), reduced amount of contrast agent (10 ml or 20 ml injected with 15 ml/s or 20 ml/s) and only one scan. After correction of the position of the patient the investigation run with two scans each was started.

It is difficult and in some cases impossible to distinguish between coronary arteries and pulmonary veins if only one image per injection of contrast material exists. Identification of these vessels is much easier if a sequence of images is recorded because the contrast material enters and leaves these vessels at different times. On the other hand it is not possible to take a long sequence of images after the injection of the contrast material because of the skin dose per image. Therefore, as a compromise, two images per injection were recorded. In the consequence that means that the scan of the patient must be started at the optimal time. A study⁽¹²⁾ has shown that the circulation times of different patients can vary from 6.8 to 24.6 s. The values depend on the pulse rate of the patient and the cardiac output, which can in some cases change dramatically during the imaging procedure. These changing circulation times can influence the quality of the images because the time interval for optimal images is small. The images must be taken about 1 s after the arrival of the contrast agent in the coronary arteries. Two seconds later the image quality is no longer satisfactory. Therefore, we measured the circulation time of the patient with a dye just before the investigation run starts. For this purpose 5 ml of Cardio Green are injected via the same catheter as used for the contrast agent. With the use of a sensor at the patient's ear and a densitometer the time between injection of the solution and its arrival in the ear is determined. This procedure has allowed the scan to be recorded at the optimal time in about 70% of the cases. More experience with this method will improve this result.

For the investigation the speed of the scanning device was adjusted relative to the measured flux in the monochromatic beams in a way that the skin dose per scan to the patient in the small field (see above) was 50 mGy. The speed varies between 9.2 cm/s and 22.0 cm/s. The time interval between the images was 1.7 to 2.2 s (depending on the scan speed).

Depending on the coronary artery of interest the patients were investigated in different projections: LAO 20°, LAO 30°, LAO 40°, RAO 30° (CC0° or CC10°) or left lateral. For the investigation runs 30 ml of contrast agent (Solutrast[®], 370 mg of iodine per ml) were injected within 2 s into the superior vena cava. This intravenous injection was performed via a 7F pigtail catheter.

Fig.2 shows the energy images of a patient in a LAO 30°-projection. The resulting subtraction image is shown in Fig.3 together with the second image of the same contrast agent injection. For comparison Fig.4 shows the same patient in a slightly different projection (LAO 40°-projection). In this case not only the right coronary artery (RCA) is visible but also part of the left anterior descending coronary artery (LAD). This demonstrates that carefully selected projections together with a wider detector could allow the visualization of left and right coronary arteries in the same image. Therefore, for the investigations in 1994 a 13.4 cm wide version of the two-line ionization chamber will be installed.

Fig.5 shows the two images of another patient in RAO 30°-projection. The LAD is clearly visible but the circumflex coronary artery (Cx) is superposed by the left ventricle

(LV) and therefore not visible. This is in agreement with a study⁽¹³⁾ which showed that the visualization of the RCA should be possible in any cases. The LAD should be visible without superposition of large structures like LV, left atrium (LA) or aorta (Ao) in 80% of the cases. Problems are expected with the main stem and the Cx.

Because it is essential for the method that all coronary arteries can be imaged, image processing methods must be used to visualize those parts of the coronary arteries which are superposed by large structures. Therefore, the right images in Figs. 3 and 5 were processed with an unsharp masking algorithm. The preliminary results are shown in Fig.6. The superposed parts are visible but the quality of these images must be increased by more sophisticated algorithms.

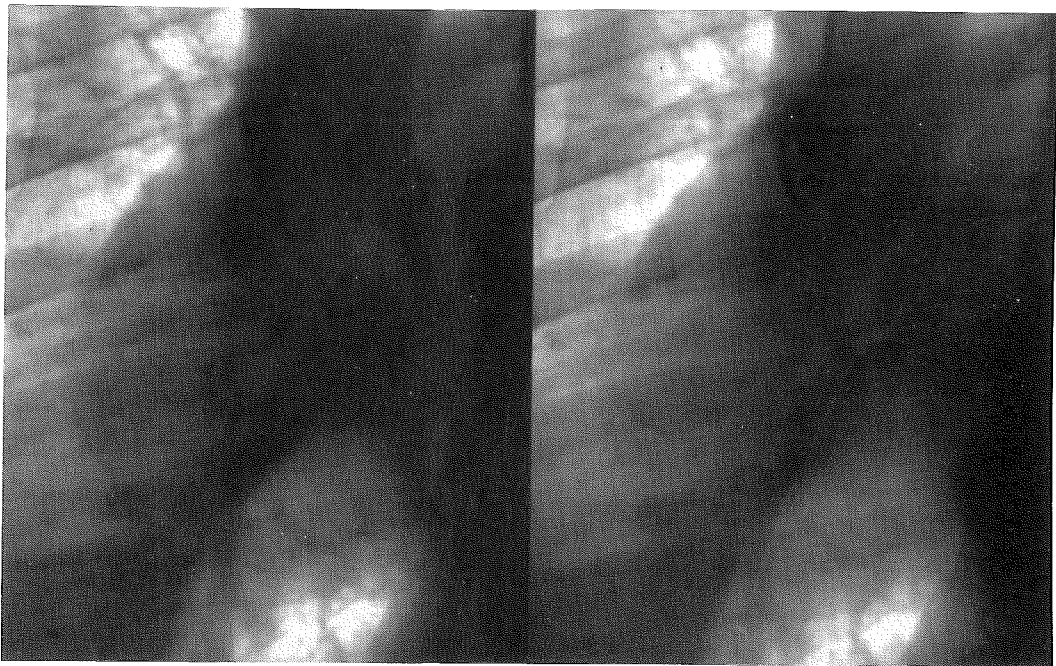


Figure 2: Energy images of a 65 year old man (65 kg) in LAO30°-projection from November 1993. The scan speed was 16.0 cm/s. The pixel size was $0.4 \times 0.4 \text{ mm}^2$. The DORIS storage ring ran with a current of 64 mA. 30 ml of contrast agent were injected via a 7F pigtail catheter into the superior vena cava within 2 s. Left side: image with energy above the K-edge of iodine, right side: energy below the K-edge. The subtraction image is shown in Fig.3 (left side).

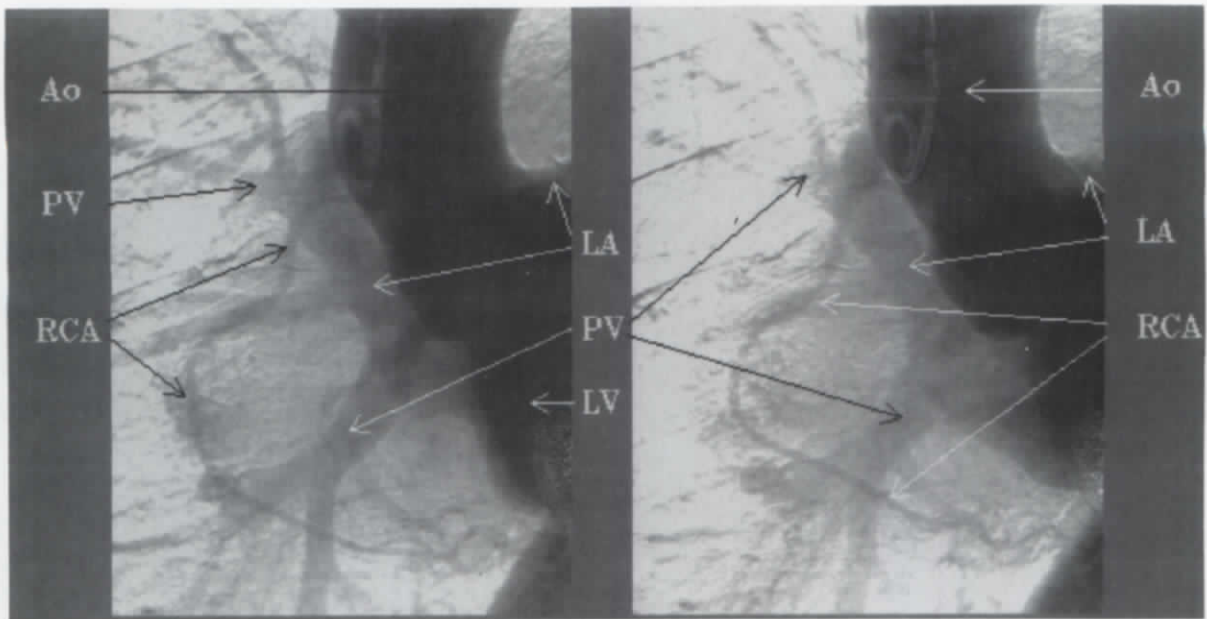


Figure 3: Intravenous angiograms of the same run. The first scan (left side) was started 14.6 s after injection of the contrast agent; the second scan (right side) was started 16.3 s after injection. The second scan was optimized for the measured circulation time. Visible are right coronary artery (RCA), parts of the aorta (Ao), of the left atrium (LA), of the left ventricle (LV), pulmonary veins (PV) and the pigtail catheter in the superior vena cava.

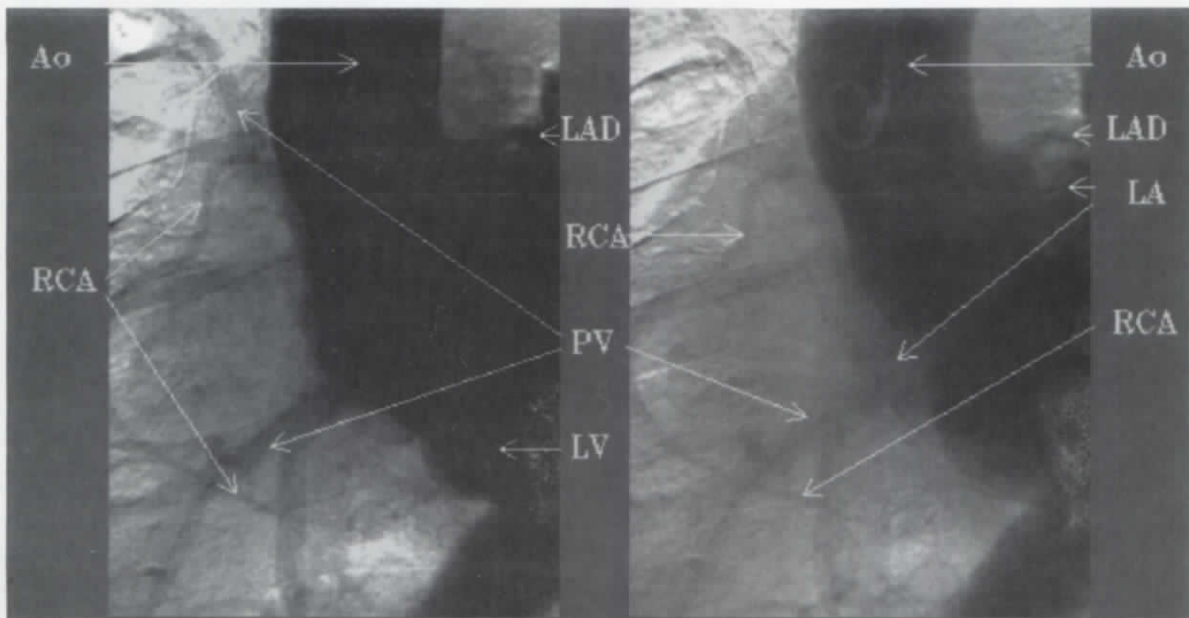


Figure 4: Intravenous angiograms of the same patient as in Fig.3 in LAO40°-projection. The parameters are the same as in Fig.3 with the following exceptions: The scan speed was 12.5 cm/s. The DORIS storage ring ran with a current of 49 mA. Visible are right coronary artery (RCA), parts of the aorta (Ao), of the left atrium (LA), of the left ventricle (LV), pulmonary veins (PV), additional part of the left anterior descending coronary artery (LAD) and the pigtail catheter in the superior vena cava.

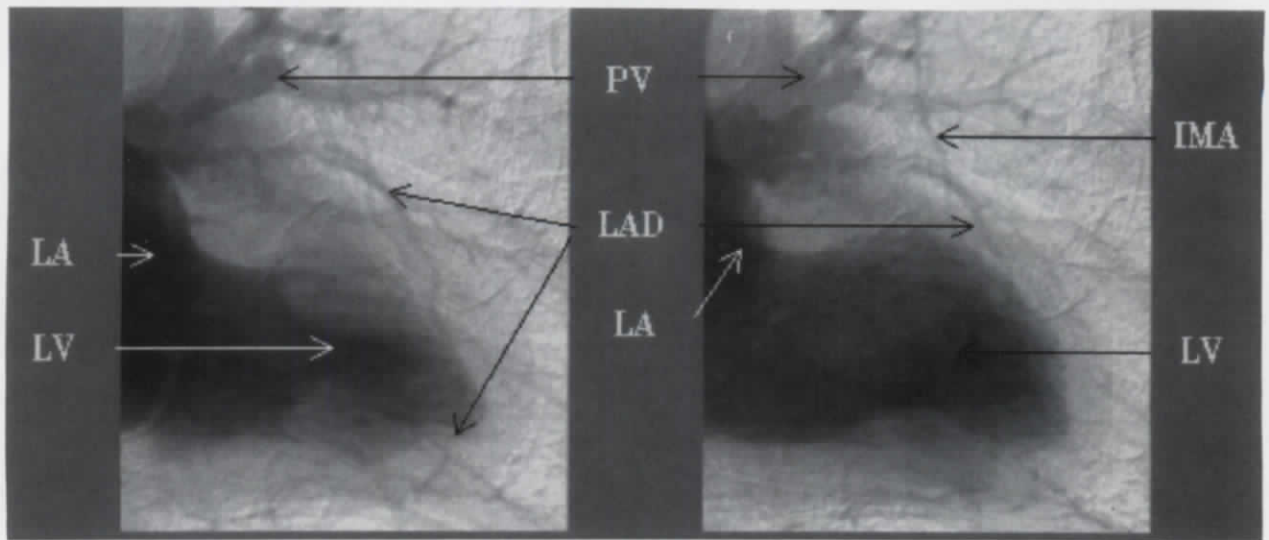


Figure 5: Intravenous angiograms of a 56 year old man (91 kg) in RAO30°-projection from August 1993. The scan speed was 16.7 cm/s. The DORIS storage ring ran with a current of 51 mA. 30 ml of contrast agent were injected via a 6F pigtail catheter into the superior vena cava within 2 s. The first scan (left side) was started 16.0 s after injection of the contrast agent; the second scan (right side) was started 17.7 s after injection. The second scan was optimized for the measured circulation time. Visible are left anterior descending coronary artery (LAD), parts of the left atrium (LA), of the left ventricle (LV), of the internal mammary artery (IMA) and pulmonary veins (PV).

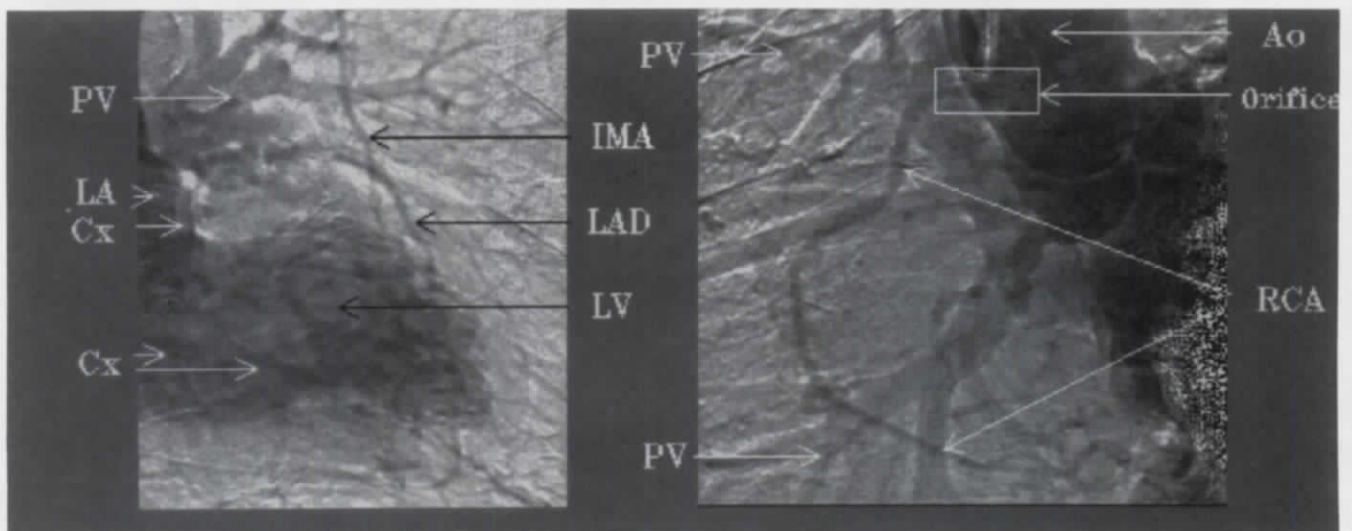


Figure 6: Intravenous angiograms from Fig.5 (right side) and Fig.3 (left side) after image processing with an unsharp masking technique. Visible are the Cx inclusive bifurcation (left side) and the orifice of the RCA (right side).

4. Outlook

A further increase of image quality without increase of skin dose is of great interest. Therefore, changes and developments in several directions were started.

A new more stable version of the monochromator will be installed before the next investigations. An increase in the flux of 20% is expected. The update of the storage ring DORIS (e^+ instead of e^-) should result in a higher current in the machine and longer storage times. Together with the installation of an advanced beam position control in the beamline the aimed flux of 3×10^{11} photons/mm²/s in the monochromatic beams in front of the patient is possible. The increased flux makes it possible to scan at 50 cm/s. This provides the opportunity to take the images in the slow motion phase of the heart, thus decreasing the blurring of the images due to cardiac motion of the heart. Furthermore the vertical smearing from the line scan will be reduced.

The installation of the new version of the detector not only increases the horizontal width of the images to 13.4 cm but also increases the dynamic range to 60000:1 and decreases the readout time per line to 1 ms. Tests must show whether the DQE can be increased from 58% today to the theoretical value of 80%. The improved parameters will increase the signal to noise ratio in the images.

The image processing work must be intensified. With new algorithms for edge preserving smoothing, corrections for higher harmonics in the monochromatic beams, system dependent corrections etc. a higher image quality must be achieved.

Furthermore the medical parameters for the investigations of patients without substantial loss of image quality will be optimized within the next two years. In detail the following parameters must be determined:

- The best projections for imaging of all coronary arteries,
- the best suited phase of the heart cycle for the images,
- the minimal amount of contrast agent,
- the maximal speed for injection of contrast medium,
- injection into the antecubital vein instead of the superior vena cava,
- optimal scan time relative to measured circulation time,
- minimal skin dose.

In a second phase the dichromography will be validated against selective coronary angiography. At the same time e.g. basic research on natural history of coronary artery disease and the study of effects of therapeutic interventions will be possible.

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