ESRF	**Experiment title:** *"Di-chromatic angiography and fluorescence imaging, a new non-invasive diagnostic method and first application for dynamic measurements of cardiac micro circulation"*	**Experiment number**: MD-134
Beam line: ID17	**Date of experiment**: from: Sept. 12, 2007 to: Sept. 19, 2005	**Date of report**: March 1st, 2007
Shifts: 17	**Local contact(s)**: Dr. Herwig Requardt	*Received at ESRF:*

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Report:

1. Overview

A total of 7 pigs have been prepared with catheters for measurements of cardiac flow dynamics using gadolinium containing contrast agent. 4 pigs could be kept under stable conditions for about 3 to 10 hours to perform successful measurements. Three different sets of measurments have been carried out to address different questions:

1. recording of stereoscopic view. For this series of measurements a special rotating support had been developed and installed.
2. perfusion mesurements at a time scale of seconds for artificially suppressed blood flow
3. blood flow in coronary arteries at a ms- time scale.

Experimental procedure

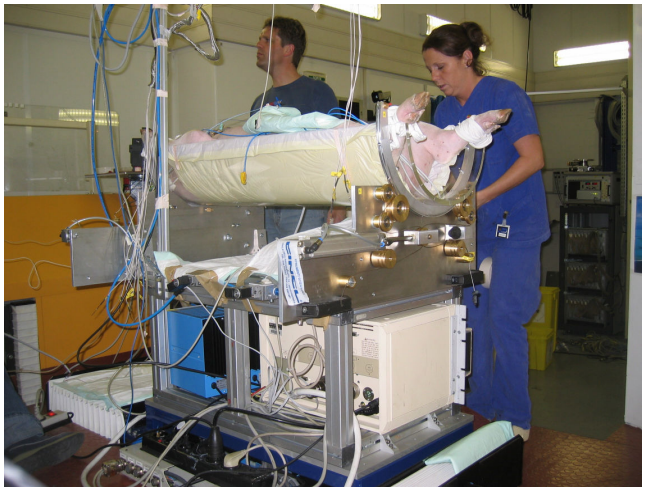


Fig. 1. Set-up for pig measurements at the beam line

Instead of the usual chair for human patients at the medical beam line ID17 a support (cradle) has been constructed to position the animal with respect to the beam such that a rotation of ± 45 ^{0} (in total 90^0) is possible a time short enough to be cariried out during the time slot (less than 1 s) between the up- and down scans (see fig. 1). The rotation is pneumaticly driven and can be triggered to fit exactly the optimum moment. The reproducibility is about ± 1 ^{0}. In the first mesurments with an animal (pig, 35 kg) it was shown that despite the quite rapid movement of the animal no stress could be observed. There was no detectable change in blood pressure or pulse rate. Images were as sharp as usual. The necessary cables and connections could be fixed without complications. The support is entirely made of lucite in order to minimize the x-ray absorption. End rings provide the necessary stiffnes.

For the perfusion measurments the heart is scanned in a sequence of up to 16 images within 30 seconds where the up- and down movement of the cradle give one image each. The contrast medium (Gadobutrol) is injected after the start of the sequence such that the full process of flow in the coronary arteries, the flow into the myocard and finally the venous back flow is visible. Fig. 2 a shows the first phase of injection in comparison to the standard angiographic porocedure in a hospital. The clear advantage of the di-chromatic subtraction angiography is seen such that the total background is removed and only the contrast medium is visible as a well distributed shadow. Although the recording of one image takes about 1 s the correspoding time slot of a selected region (ROI) is much shorter. Therefore the measuerment of the contrast in a given frame represents a rather precise sampling of the concentration of the selected view. As region of interest ROI 1 an area at the end of the (fig.2 c, upper) and as reference an area ROI 2 on the opposite side is selected. The result of an artificial obstruction inflating a balloon in the LAD (white arrow left upper image) is a reduction of perfusion (middle image) and after deflation the reperfusion is seen (right upper image). The color coded images (lower row) make it even easier to localize by eye the perfusion. A quantitative analysis (2c, lower images) show the lack of perfusion in the early phase and an overshoot after reopening. The control area shows no change of signals.

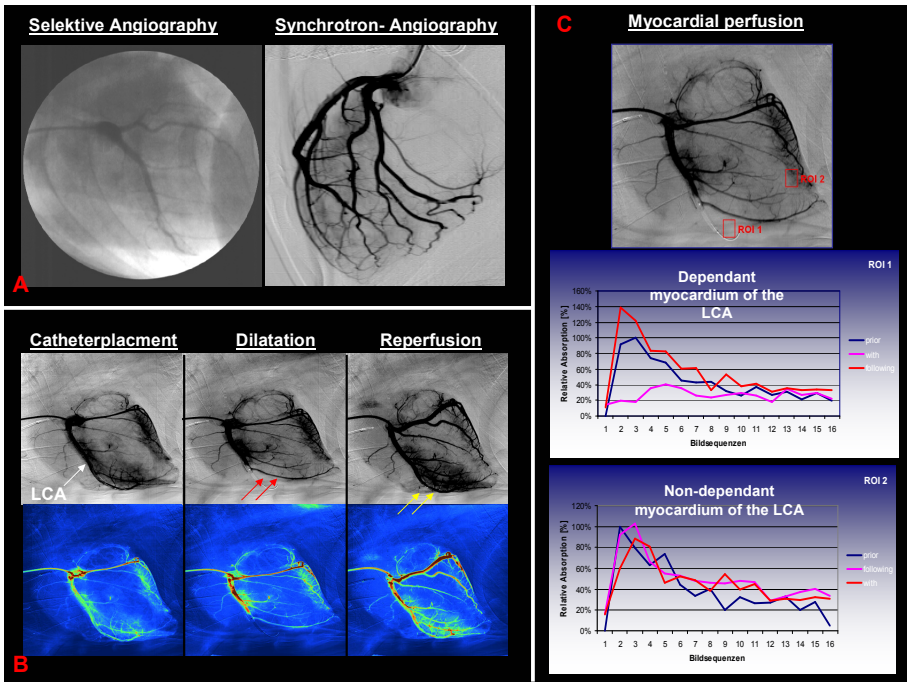


Fig. 2. measurment of perfusion dynamics:a)projection image b) perfusion before,during and after balloon dilatation c) upper: ROI, lower: time dependent contrast

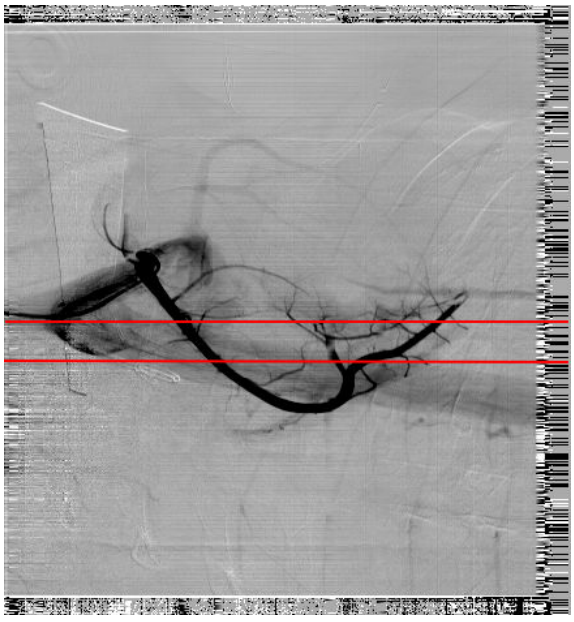
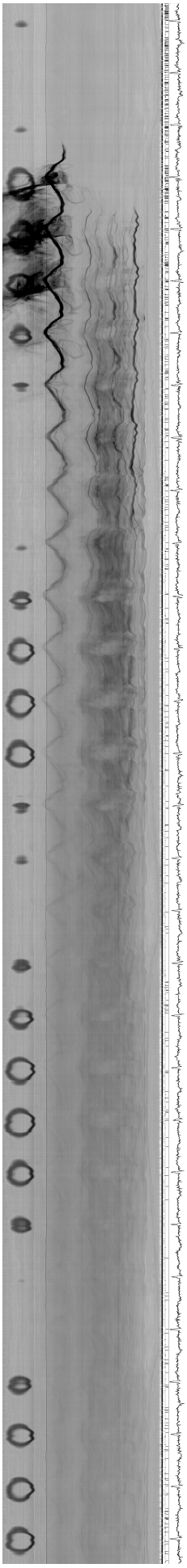


Fig. 3. Projection image of coronary artery and indication of recorded lines

The third measurment records the change of contrast medium in the coronary arteries at a much shorter time scale such that the movement of the injected bolus is clearly visible. It is speculated that with this method of "first pass" measurement ultimately the flow, possible restrictions and the quantitative assessment of the overall flow dynamics including the perfusion should be possible. As compared to other methods working in a similar time scale (Doppler probes, pressure sampling), the synchrotron method allows an easily accessible measurement of flow with imaging quality, thus having the potential for a differential diagnosis of the status of the heart function. In order to preserve this important imaging quality at the very high time resolution (≈ 4 ms resolution) a new scanning procedure (Time Projection Imaging, TPI) was tested. The animal is positioned such the the fan beam crosses the heart at a given position (fig.3a). The Germanium detector of ID17 records as usual this line. Since the object does not move the detector records avery 4 ms a new line reproducing the change of contrast in the arteries in the field of view. Since the coronary arteries move synchronously with the heart beat the detector records meandering vessel structures (fig. 4). Although the



spatial coordinate is in the horizontal axis and the vertical axis represents the time scale (including at the faremost richt the ECG signal), it is noticed that arteries are easily recognized as continous structures, even smaller ones. Sometimes vessels enter the field of view and sometimes they leave it producing special structures. At the top the injection of the bolus as a sharp begin of the dark line is visible. After some time the darkening (concentration of contrast medium) diminishes as the contrast medium flows out of the arteries. Between the vessels slow darkening and bleaching is noticed reproducing the time dependent perfusion of the heart muscle. The fact that this separation of major vessels and smaller structures as arterioles and capillaries is astonishingly clear is already viseable in fig. 2a (right) and c and is not visible in fig. 2a (left) taken with standard x-rays. The challenge after this discovery is the quantitative interpretation of the data. In a first trial an imaging program has been used by interactive "vessel finding" to produce the intensity profile along the time axis. Fig 5 shows for the main artery (upper line in fig.3, closest artery to the aorta) clearly the beginning of the bolus and the modulation produced by the heart beat.

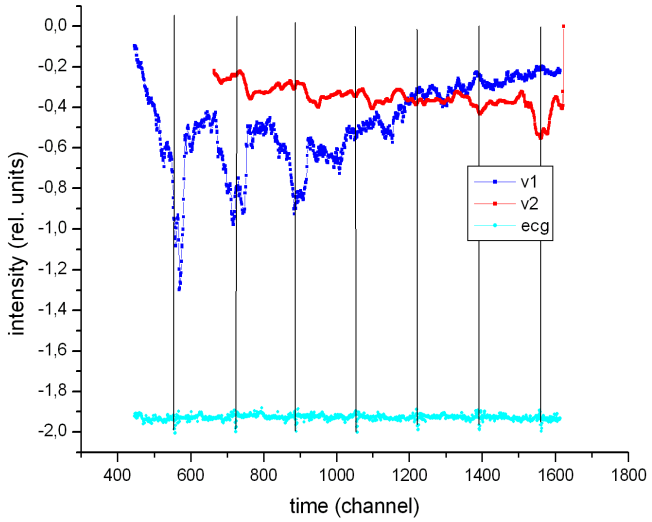


Fig. 5. Intensity along the coronary arteries 1 and 2. Lower curve: ECG

Conclusion

The measurments show clearly the advantages of the synchrotron radiation for fast time resolved measurments as well for perfusion as for flow dynamics.

The data from the stereo images have not yet been anaylsed, since the analysis of the two other subjects has priority. In addition, the data from fig. 2 and 3-5 are of such good quality that the anticipated reconstruction of the structures is not imminently necessary. The quantitative interpretation of the data given in fig. 5 including the substructurs during a heartbeat needs quite some detailed development of software and interpretation of models for flow dynamics. For example, it is already visible that the vessel further down (vessel 2) has a completely different substructure. First ideas of interpretation suggest the inclusion of a non-linear diffusion model. It will be discussed in the forthcoming report.

Fig. 4. Time Projection Imaging. Recording of a single line of fig.3 (horizontal axis) as funtion of time (vertical axis)