

# Pressure Controlled Intermittent Coronary Sinus Occlusion – an Alternative to Retrograde Perfusion of Arterial Blood<sup>1)</sup>

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**Summary:** Conflicting reports of the arterialisation of the coronary sinus led to the development of pressure controlled intermittent coronary sinus occlusion (PICSO). Unlike arterialisation methods, this form of treatment does not include retroperfusion of blood. We suggest that redistribution of flow and pressure into ischemic areas occurs on a microcirculatory level. The coronary sinus pressure serves as control parameter allowing optimal redistribution and sufficient drainage of the coronary venous system. The effectiveness of this intervention could be proved in several experimental series. The mechanism of action is suggested to be washout of toxic metabolites and myocardial edema. A hyperemic response in coronary arteries during the release phase of the occlusion might be another important factor for the salvage of jeopardized myocardium. Coronary sinus pressure parameters do not only allow a physiologic counterpulsation but give insight into various hemodynamic and even prognostic factors otherwise undetectable. The development from hypothesis to first human trials is presented.

Many publications concerning arterialisation of the coronary sinus have been repetitious in the interpretation of results. Changes of the myocardial structure and coronary vasculature induced by permanent arterialisation of the coronary sinus have been adopted for permanent coronary sinus occlusion. However, the hazard of permanent coronary sinus occlusions seems to be different and jeopardizes myocardial perfusion before a considerable engorgement of the heart occurs. Intermittent coronary sinus occlusion (ICSO) and especially pressure controlled intermittent coronary sinus occlusion (PICSO) is conceptualized to minimize severe side effects and maximize the benefit for acutely injured myocardium. The scheme adopted in this presentation is to show in a chronological manner the development of PICSO from imagination to first human trials.

The development of pressure controlled intermittent coronary sinus occlusion (PICSO) was begun to prove the hypothesis stating that “arterialisation of the coronary sinus results in an alteration of flow and pressure in the microcirculation of the heart”. Improvements in the ischemic myocardium should therefore be possible only by intermittent occlusion of the coronary sinus. We evaluated this hypothesis and were able to show a substantial infarct size reduction, an improvement of regional myocardial function as well as beneficial effects on myocardial metabolism. Furthermore, we were able to identify washout of toxic metabolites and myocardial edema as mode of action of this intervention. The use of coronary sinus pressure as control parameter for the periodic change of venous drainage makes possible the computation of hemodynamic parameters and the time

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course of the ischemic process. Most important, however, we report on the first human series treated with PICSO showing similar results as proposed in our experimental investigations. We believe that this intervention is the only physiologic approach to improve myocardial ischemia via the coronary sinus. This article summarizes the motivation, the highlights, and the drawbacks of our research in chronological order, as well as remaining questions for further research.

### **The Idea of Intermittent Coronary Sinus Occlusion**

In my second year as resident surgeon in 1976, Professor Moll from Lodz (Poland) visited the 2nd Chirurgische Universitätsklinik in Vienna to report on his human trials of the permanent arterialisation of the coronary sinus in patients with severe diffuse coronary heart disease. Taking note of experimental and anatomic findings of E. Pakalska from Lodz, who demonstrated the possibility of treating myocardial ischemia by arterialisation of heart veins, Moll started the above arterialisation in patients with disseminated arteriosclerotic changes in 1972. In 52 carefully selected patients representing 2% of surgically treated patients with coronary heart disease, the anterior descending or great coronary vein was anastomosed with the internal mammary artery because of good correlation between the wall thickness and the diameter of the vessels. Long-term clinical results (34 patients) as well as the data obtained in cooperation with M. Edelman showed the good general state of health, normalisation of the ST-depression, diminished heart size, and a patent bypass. Moll concluded that in a small but identifiable group of patients, where direct revascularisation is impossible, the arterialisation of coronary veins should be taken into serious consideration.

I was fascinated by the idea cited above, to use the coronary sinus as access to deprived myocardium. On the other hand research was stimulated by the obvious discrepancy of retroperfusion of arterial blood engorging the heart and jeopardizing normal coronary circulation. The success of the originality of research was enabled by two major factors: the challenge to find evidence for a proposed hypothesis that pressure and flow changes induce similar beneficial effects as permanent arterialisation without severe side effects; and secondly, we left our work uncompromised by earlier reports (not intentionally but by chance). Otherwise our research would have followed the deductive evidence of work that has been done starting in 1930. When we became aware of this work, our experimental results of pressure controlled intermittent coronary sinus occlusion showed a strong individuality so that further evaluation was justified (1–17).

### **The Concept of Pressure Controlled Intermittent Coronary Sinus Occlusion**

Intermittent coronary sinus occlusion (ICSO) is a time dependent blockade of the coronary sinus. The concept to use the coronary sinus pressure as control parameter for coronary sinus occlusion times developed over several years and was first published in 1980 [1]. The use of the coronary sinus pressure as feedback control allows the most physiologic approach to improve ischemic myocardium, since coronary sinus occlusion allows an even distribution of pressure and flow towards jeopardized zones according to the pumping efficiency of healthy myocardium. Continuous employment of PICSO altered the

concept to a pressure and flow controlled intervention based on the experience that coronary sinus occlusion produces a hyperemic response on the arterial side of the coronary circulation. Optimization criteria for this intervention are now under investigation.

### **Chronological Order of Experiments**

In the beginning it was very difficult to obtain the interest of scientific authorities and money to perform pilot experiments. First trials with an open chest model in sheep and dogs did not show convincing results. Furthermore lack of technology of pump systems and catheters forced us to perform coronary sinus occlusion rather than intermittent occlusions. In September 1979 we were funded by J. Herdlicka and W. Herdlicka and performed coronary sinus occlusion in closed chest dogs. It was the beginning of the balloon dilatation procedure, and a fellow cardiologist, O. Pachinger, helped us to occlude the LAD branch with a dilatation catheter and the coronary sinus with a normal Swan-Ganz catheter. In our first recordings we observed an increase of the postocclusive LAD pressure induced by coronary sinus occlusion. At that time I visited several companies to ask for technical support, especially for a modification of catheters, with only minor success. The consequence of these visits were that we still had to use latex balloon catheters, which burst almost twice in each experiment. The pump unit was a self-constructed DC driven hydraulic device with a lot of technical problems. At that time, in spring 1980, I met Professor Kessler from the physiological department of the University of Erlangen. In a collaborative effort a series of experiments studying the behaviour of tissue parameters was conducted (1). We evaluated myocardial tissue oxygen, extracellular potassium levels, and myoglobin saturation in dogs with high collateralisation. I think everybody was discouraged, because myocardial oxygen tension did not increase. However, we saw a favourable increase of the myoglobin saturation in the center of infarction. An adequate interpretation of these results was made possible by density measurements a couple of years later.

The effect of an intervention like ICSO on regional myocardial function is rather important, which was investigated in a collaborative effort with W. Heimisch and S. Hagl in the German Heart Center, Munich. I was glad to be accepted to work in the experimental laboratories of the German Heart Center. Since evaluation of regional myocardial function with sonomicrometry meets highest standards in this institution, it was easy to apply ICSO in a well-known experimental model. It turned out to be more difficult to convince my coworkers of the proposed mode of action, however, after gathering all the results some scepticism could be quashed. In those days I was a travelling researcher, because approximately at the same time we investigated the effect of ICSO on the reduction of infarct size. Although we had tried to measure infarct size previously the expertise of D. Glogar was very useful, who had just returned from a one year postdoctoral research exchange grant. At the ACC meeting in Atlanta, Georgia, in 1982, and at several European meetings we reported on beneficial effects of this intervention. After completing these experiments we were in the position, although knowing interpretations of earlier and contemporary work, to resist counsel that clashes with conviction. At that time we suggested that only the redistribution of blood into ischemic areas and the increase of perfusion

were the modes of action of PICSO. However, this is only partly true. Negative studies of effects of PICSO (we chose PICSO as pressure controlled intermittent coronary sinus occlusion to discriminate time dependent ICISO from our intervention with pressure feedback) (18, 19) on regional myocardial blood flow showed that there has to be another mechanism involved.

We had some major concerns about PICSO. Does PICSO induce an edema formation and is this intervention harmful to endothelial cells? We tried to investigate prostaglandines, but we were not very successful with the interpretation of widely scattered data. To investigate the problem of the edema formation, a very important and close cooperation was formed with Professor Kenner and Dr. Moser from the Physiologic Institute of the University of Graz. Kenner and Moser are not only experts in the field of microcirculation of the heart, but were also working on a new method to investigate fluid shifts in the coronary circulation. It was therefore our mutual interest to apply the so-called continuous blood density measurements to evaluate effects of PICSO on the coronary microcirculation. Surprisingly enough on looking at density measurements we found out that something like washout occurs during the periodic change of the coronary sinus pressure. It is to the credit of Kenner and Moser that my intuition of washout (it was, as Konrad Lorenz would have put it, a fulguration) became more and more substantiated. From that time on I understood our experiments with the reoxygenation of myoglobin induced by this intervention obtained in experiments a couple of years ago. Understanding fluid shifts by PICSO resulted in a step by step solving of the puzzle. The milking effects of the erectile venous vasculature on the interstitial space combined with oncotic and electrochemical forces seem to produce a decrease of the diffusion distance between collateral perfused oxygenated blood and myocytes washing out edema and toxic substances, resulting in an improvement of regional function and structural salvage.

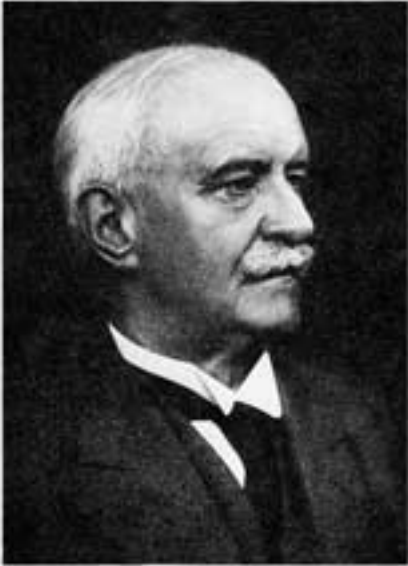
Most of the studies that followed were designed to optimize the efficiency of this intervention, to learn about the physiologic consequences of coronary sinus occlusion and to evaluate the information about coronary sinus pressure.

Nowadays, the challenge is to validate this intervention. Therefore it was very important that the group of J. Hopkins was able to corroborate our results on infarct size reduction. An excellent working relationship was established with S. Meerbaum, E. Corday, A. Jacobs, C. Punzengruber, D. Faxon and A. Aigner, including collaborative efforts in canine experiments.

It was the hypothesis of washout that justified our first human trials of PICSO. In June 1983, 15 patients undergoing aortocoronary bypass grafting were asked to participate in the study. The results presented in this book convincingly show the potential of PICSO also in a human setting. We are now up to calling for a randomized intraoperative study on PICSO to learn more about this promising technique and to convince the scientific community that PICSO is effective to protect human myocardium jeopardized by global ischemia and reperfusion.

The challenge for the future, however, remains the understanding of which changes induce redistribution of plasma and blood (as with PICSO) into deprived myocardium on a molecular level. It is very likely that not only the research of C. Beck but also of A. Bier (Fig. 1), who invented the so-called hyperemia by venous stasis will gain rejuvenation of interest (20).

Ongoing research of our group partly published in this paper is trying to shed light on several aspects, such as effects of PICSO on high energy phosphates and cellular metab-



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olism, on optimization criteria, diagnostic features of the coronary sinus pressure rise, and on the improvement of the knowledge of the mode of action of PICSO, as well as the hyperemic response induced by PICSO. With the present knowledge of PICSO we are convinced that this intervention will be part of the standard therapy in acute myocardial ischemia and secondly will enhance our knowledge of coronary heart disease.

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