SUMMARY AND DISCUSSION

In this thesis several aspects of passive and active coronary perfusion during coronary angioplasty are investigated. The autoperfusion balloon catheters that were evaluated are the Stack® and the RX-60® catheters (Advanced Cardiovascular Systems, Inc., Santa Clara, California, U.S.A.). The coronary perfusion pump was a specially designed piston pump (Leocor, Inc., Houston, Texas, U.S.A.).

Pressure - blood flow relationships in autoperfusion catheters and with the perfusion pump were studied in 2 in vitro studies. A third in vitro study was dedicated to the evaluation of mechanical hemolysis in the new active perfusion system, using 2 different catheter types, a tapered catheter and a catheter with distal side holes.

Several clinical studies were performed. In 1 study, we evaluated the efficacy of prolonged perfusion balloon angioplasty in the treatment of acute and threatened closure, the angiographic restenosis rate after successful autoperfusion angioplasty and the number of cases in which autoperfusion balloon catheters facilitated the use of arterial bypass grafts when emergency CABG could not be averted. We compared the efficacy and the impact on major clinical endpoints of perfusion balloons versus stents in the treatment of acute or threatened closure. Finally, the extent of ischemia reduction that could be achieved with the active perfusion system and its safety were investigated in patients undergoing elective angioplasty.

An overview of active and passive coronary perfusion techniques is presented in chapter 1. Andreas Gruntzig already had advocated the use of pumps to maintain distal perfusion during coronary angioplasty. However, this concept was abandoned when subsequent clinical experience revealed that inflations of 20 - 30 sec. duration were well tolerated by most patients and that coronary stenoses could be dilated effectively with this inflation strategy.

In 1985 a reperfusion catheter was developed by Hinohara and co-workers. This catheter allowed for some distal coronary flow. This resulted in a reduction of signs of myocardial ischemia when the catheter was placed across the lesion in the setting of acute or threatened closure. The reduction of ischemia facilitated the use of arterial bypass grafts during emergency surgery for this complication.

The development of the autoperfusion balloon catheter by Erbel and colleagues, was a logical next step. Acute and threatened closure are generally caused by intimal dissection and it now became possible to effectively ‘tack up’ intimal dissections through prolonged balloon inflation. This resulted in a reduction of the need for emergency bypass surgery by 65 - 80%. When compared with stent implantation for acute or threatened closure, the initial success rate of stenting appears to be higher than the success rate of prolonged perfusion balloon angioplasty. However, there appears to be a higher subacute reclosure rate after
stenting, reducing the clinical success of this procedure. Flow rates through autoperfusion balloon catheters have only been scarcely documented. The rates for different perfusion balloons, that are available in the literature are presented in this chapter.

Several active perfusion strategies are currently available. Ischemia reduction during coronary angioplasty can be achieved with coronary sinus retroperfusion. This system has the disadvantage that it will only provide a limited reduction of ischemia because of the existence of a venous network named after its discoverer Christian Thebesius. This network drains into ventricular and atrial chambers, reducing the amount of oxygenated blood that is delivered to the myocardium. Active perfusion with Fluosol® results in only limited ischemia reduction because of the limited oxygen carrying capacity of the fluid. Additionally, this perfusion strategy will cause fluid overload if maintained for long periods. Active antegrade perfusion of blood can be achieved by manual injection, roller pumps, angiographic power injectors and with the piston pump evaluated in this thesis. Manual injection precludes prolonged perfusion because of operator fatigue. Roller pumps will slip, and this results in a reduced flow rate. Power injectors have to be prefilled with heparinized blood and their volume of 500 cc limits the perfusion time. Data about the efficacy and safety of the piston pump are scarce. There is only 1 well documented clinical study, demonstrating effective ischemia reduction compared to standard PTCA.

Because of the limited blood flow rate data available in the literature, we investigated the blood flow rates through the Stack® and RX-60® autoperfusion balloon catheters. This study is presented in chapter 2. In vitro, under different continuous pressure regimens, the flow rates were dependent upon catheter dimensions, but also on blood viscosity and temperature. Additionally, the experimental setup played a role. If a hemostatic valve was used to seal the blood reservoir, it narrowed the through lumen of the catheter, resulting in reduced flow.

The extrapolation of the flow rates obtained in vitro, to the clinical situation in patients, remains troublesome. In patients the flow will be essentially diastolic due to the phasic nature of coronary flow. Additional factors like distal coronary resistance and obstruction of the side holes by the vessel wall and/or clots will further reduce the flow. A flow rate of 60 ml/min, appears to be sufficient to abolish ischemia during angioplasty of most segments, when no side branches are occluded during balloon inflation (1). Hence, the rate of 75 ml/min. that was measured through the Stack® catheter should be enough to prevent the occurrence of ischemia. However, due to the factors mentioned above, the flow rate in patients will be lower. This is also in accordance with clinical observations. Muhlestein and colleagues observed mild to severe angina in 20% of patients undergoing prolonged autoperfusion balloon inflation (2). Seggewiss and co-workers observed the same in 42% of their patients (3).
In chapter 3, the driving pressures and blood flow rates through the Stack® autoperfusion balloon catheter that were measured in the experiments described in chapter 2, were compared to pressure and flow during perfusion with the pump. The flow through the autoperfusion balloon catheter was markedly higher at significantly lower pressures, than the pressures that were necessary to perfuse blood through the angioplasty catheter with the pump. The shorter perfusion channel (approximately 15 cm) and the wider lumen of this channel (0.9 mm compared to 0.8 mm proximally and 0.5 mm distally in the active perfusion catheter) are the main factors responsible for this higher flow rate. When the active perfusion system is applied in patients kinks and curves in the catheter will further increase the flow resistance. If the hemostatic valve at the proximal end of the guiding catheter is closed too tightly, it will narrow the through lumen of the perfusion catheter, resulting in a further increase in flow resistance.

Nevertheless, due to factors mentioned previously, it appears that the flow through autoperfusion catheters in patients, will be significantly lower than in these in vitro experiments. The major advantage of the perfusion pump appears to be that it should be able to provide a flow of 60 ml/min. independent of the patients blood pressure. This is of special importance in patients who are in cardiogenic shock secondary to acute or threatened closure and in patients undergoing angioplasty with a high risk of hemodynamic collapse during balloon inflation. Additionally, obstruction of the side holes in the autoperfusion balloon catheter cannot be ruled out when the catheter is left in place for longer periods (e.g. 1 - 2 hours) during preparation for emergency bypass surgery. This clot formation will further reduce the flow through the catheter. The active perfusion catheter that is currently used with the pump does not have side holes. Therefore, the risk of clot formation in this catheter appears to be lower than in the autoperfusion catheter.

Chapter 4 presents the results of in vitro hemolysis tests during active perfusion. Fresh human blood was perfused through the system at different flow rates. Samples for hemolysis testing were collected after 1 min. at each flow rate. Two PTCA catheter types were evaluated in combination with the pump. Both catheter types were 135 cm long. One catheter type had a through lumen of 0.8 mm and 6 distal side holes. The other catheter was a tapered catheter without side holes but with a proximal 127.5 cm through lumen of 0.8 mm and a distal 7.5 cm lumen of 0.5 mm. The active perfusion system exhibited several mechanical factors that may cause hemolysis. Shear stress in the distal part of the tapered catheter was >200 Pascal, positive pressure was >3 atmospheres and the flow in the pump was turbulent (4.5). Additionally, the pump has occlusive valves that will compress blood cells. Nevertheless, no significant increase in any of the biochemical markers of mechanical hemolysis was observed. This can be explained by the short period during which the blood was subjected to mechanical factors that cause hemolysis,
because mechanical hemolysis is time dependent (4). Additionally, the pump volume is small, hence the prosthetic surface with which the cells interact, is small. Finally, the volume of blood in the pump itself is small and only 0.5% of red cells will actually hemolyze upon contact with a prosthetic surface (6). Hence, there is a small volume of blood subjected to contact with a small prosthetic surface for a short period of time. These appear to be the major reasons why hemolysis was insignificant in these experiments.

In these in vitro experiments, the major factors contributing to thrombus formation were: platelet activation, flow rate and contact activation of the clotting cascade. In all the experiments in which the 'side hole catheter' was used, the catheter became obstructed with clots. The side holes cause a jet effect with turbulent flow because their diameter is narrower than the catheter lumen. This turbulent flow may cause platelet activation. Subsequently the platelets may become trapped between the catheter and the inner surface of the tube that contains the catheter, because the flow in this area will be much lower than in the catheter lumen (the transmission of an effective driving pressure is hindered by the narrow side holes). No increase in thromboxane B2 was observed. Most probably, the activated platelets were trapped in a clot that initially remained outside the catheter. Eventually, this clot must have propagated rapidly into the catheter lumen causing obstruction, and precluding the measurement of increased thromboxane B2 levels at the catheter tip. We concluded that side holes in a catheter do not reduce the flow resistance during active perfusion. On the contrary, resistance is increased because of the formation of obstructive clots.

In these experiments, the samples were taken after 1 min. at each flow rate. It remains to be seen if hemolysis remains negligible when the pump is used for longer periods of time, e.g. during preparation for emergency surgery. Additionally, as was mentioned above, the flow rate plays an important role in the propensity for clot formation in the system. We are currently conducting a series of experiments in a pig model. In these experiments, passive and active perfusion are compared during PTCA of the left anterior descending coronary artery. We observed the formation of clots on the inlet valve of the pump during a perfusion period of 20 min. at a flow rate of 20 ml/min. These clots impaired adequate closure of the valve. During the ejection phase the blood was perfused back into the catheter through which it had been aspirated during the aspiration phase. The flow through the left anterior descending coronary artery was measured with a clamp on doppler flow probe. There was only minimal (3 - 5 ml/min.) flow in the coronary artery and the electrocardiogram showed pronounced ST-segment elevation. The animal, which weighed 31 kg, had been adequately heparinized (2 times 5,000 units in 30 min.).

Indeed, the most likely place for clot formation appears to be the disposable ‘pump head’ that fits on top of the battery operated driver (see figures 1 and 2 in chapters 3 and 4 respectively). Flow in this part of the system is turbulent and it

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SUMMARY, DISCUSSION AND CONCLUSIONS

Initially, the pump and its cells interact, is only 0.5% of red blood cells (6). Hence, for reasons why the clotting was used, the jet effect with lumen. This platelets may the tube that is hindered by observed. Most remained rapidly into the extent of increased side holes in a. On the contrary, it is therefore not unlikely that valve dysfunction with reduced pump flow will remain unnoticed until the patient experiences severe signs of myocardial ischemia. This would put the patient at risk, especially during application of the system for bail out PTCA in a proximal lesion of a large coronary artery or during elective high risk angioplasty.

Based on the in vitro experiments and the animal experiments mentioned above, it would seem desirable to reduce the risk of clot formation in the system. The design of the ‘pump head’ may be changed in such a manner that there are less areas in which turbulence may occur. Additionally, the propensity for thrombus formation may be reduced by applying a non-thrombogenic coating.

Chapter 5 focusses on the efficacy of autoperfusion balloon catheters in the treatment of acute or threatened closure. In 40 patients an autoperfusion balloon was used to treat acute or threatened closure. They would all have been candidates for emergency surgery if the perfusion balloon had not been available. Success was defined as a stable stenosis < 50% with flow grade 3 according to the scale of the thrombolysis in myocardial infarction (T.I.M.I.) trials grading system. There also should be complete resolution of all signs of myocardial ischemia. Success could be achieved in 65% of the patients.

The majority of patients in whom emergency surgery could not be averted received arterial grafts. The hypothesis that the perfusion balloon facilitated the use of arterial grafts during emergency surgery is supported by the results of emergency CABG in a prospective control group (31 patients). This group consisted of all patients who underwent emergency surgery for failed PTCA after the introduction of routine use of arterial bypass grafts in our center, but before the availability of the perfusion balloon. There were no significant differences in clinical characteristics between this control group and the patients who were treated with a perfusion balloon. All patients in the control group received venous grafts. It therefore seems reasonable to assume that the flow through the autoperfusion balloon catheter may have stabilized the patients to such an extent that arterial bypass contains 2 occlusive valves. It seems likely that there is a jet effect distal to the inlet valve, because there is transition from the inlet tube through the valve into the wider chamber of the ‘pump head’. The fact that in the animal experiment mentioned above, the clot developed on the inlet valve supports this notion.

The most likely consequence of clot formation in the ‘pump head’ appears to be valve dysfunction as observed in our experiment. The risk for embolization into the PTCA catheter and subsequently into the coronary artery may be lower, because the clot may not pass the valves. As the clot has developed in the chamber of the ‘pump head’, it seems likely that it will be too large to pass the valves. Nevertheless, valve dysfunction in itself is a serious complication because it significantly reduces pump flow. The pump lacks any means of direct flow measurement (e.g. a clamp on doppler probe on the tube leading to the PTCA catheter). It is therefore not unlikely that valve dysfunction with reduced pump flow will remain unnoticed until the patient experiences severe signs of myocardial ischemia.
grafts could be used more often during emergency surgery than before the availability of this device. Our study is the only study that has investigated whether there was an increased use of arterial grafts during emergency surgery with the support of the autoperfusion balloon catheter. Our findings are in accordance with the earlier experience with the reperfusion catheter described in chapter 1. This catheter also facilitates antegrade flow during preparation for emergency surgery for failed PTCA. An increased use of arterial grafts during emergency CABG with the support of the reperfusion catheter has been documented by Sundram and co-workers (7).

When the autoperfusion balloon became available in our center, restenosis after successful application of this catheter had not been studied. We found an angiographic restenosis rate of 42%, which is at the upper end of the normal limit (8,9). A factor contributing to this relatively high restenosis rate may have been the persistence of intimal flaps in some patients in whom a satisfactory luminal opening could be achieved with the perfusion balloon. These flaps may cause turbulent flow which may lead to platelet aggregation. Mural thrombi, resulting from platelet aggregation are considered to be a mechanism in restenosis (10,11). It must be kept in mind, however, that our patient group is too small to make any valid conclusions about restenosis after successful treatment of complicated PTCA with a perfusion balloon. Unfortunately, there is no other study with systematic angiographic follow-up after successful perfusion balloon angioplasty.

The minimum total inflation time that is required to successfully treat complicated PTCA with a perfusion balloon, appears to be 10 - 20 min. Seggewiss and co-workers found that 25 out of 26 patients (96%) who underwent a total inflation time of 10 - 20 min. were successfully treated, while success could be achieved in 17 of 23 patients (74%) with a total inflation time < 10 min. (3). The median total inflation time in our patient group was 27.5 min. (range 10 - 180 min.) with a median of 2 inflations (range 1 - 5). Our success rate was lower however (65% versus 83%). This may be explained to some extent by differences between the patient groups. We excluded patients from our study, who underwent PTCA for chronic total occlusions, because these patients generally tolerate longer inflations with a standard balloon. Additionally, 7 patients in our population were in cardiogenic shock at the moment of insertion of the perfusion balloon (they also received an intra-aortic balloon pump). These patients were almost certainly referred earlier for surgery than those who were in a stable hemodynamic situation. Hence, the presence of shock in some of our patients may explain why a larger percentage of our patients underwent surgery compared to the group described by Seggewiss et al.

Extremely long inflations as reported by Van der Linden and colleagues, do not appear to result in a higher procedural success rate and a lower complication rate (table IV, chapter 1).
Autoperfusion balloon catheters and stents are compared in chapter 6 regarding their efficacy in treating acute or threatened closure and their impact on major clinical endpoints. This study was a non-randomized prospective comparison of both treatment modalities. The use of an autoperfusion balloon or a stent was left to the discretion of the operator. Success was defined as a stable stenosis < 50%, with TIMI grade 3 flow and complete resolution of all signs of myocardial ischemia. There also should be no in-hospital reclosure or restenosis.

An autoperfusion balloon catheter was used in 61 patients and 36 patients received a stent. The groups were comparable regarding their baseline clinical characteristics including angiographic lesion morphology before standard angioplasty and before perfusion balloon angioplasty or stent implantation. The initial success rate with perfusion balloons was lower than with stents (20% versus 94%). There were no deaths after perfusion balloon angioplasty, while 3 patients died in the stent group. Emergency surgery was performed in 13 (21%) perfusion balloon patients versus none of the stent patients. Subacute reclosure during hospitalization occurred in none of the perfusion balloon patients versus 8 (24%) stent patients. Therefore, the percentage of patients with successful stent implantation at discharge dropped to the same level as the percentage of patients with successful perfusion balloon angioplasty (72% versus 70%). There was no significant difference in the number of myocardial infarctions and the enzymatic infarct size between the groups. There was no significant difference in event free survival during 3 months follow-up and there was no significant difference in angiographic restenosis.

In a separate report we have presented the costs per patient associated with perfusion balloon angioplasty versus stent implantation for acute or threatened closure (12). The costs were calculated at the end of the 3 months follow-up period. We counted the number of days that the patients were hospitalized after perfusion balloon angioplasty or stenting. We counted the number of repeat angiograms, the number of redo PTCA's and the number of patients that underwent bypass surgery. At the end of 3 months follow-up the median duration of hospitalization was 4 days (range 2 - 22 days) in the perfusion balloon group and 13.5 days (range 2 - 49) in the stent group. There were 7 (12%) repeat angiograms in the perfusion balloon group versus 16 (44%) in the stent group. There were 3 (5%) redo PTCA's in the perfusion balloon group versus 12 (33%) in the stent group. Seventeen (28%) patients had undergone bypass surgery in the perfusion balloon group versus 5 (14%) in the stent group. The differences in duration of hospitalization, the number of repeat angiograms and the number of redo PTCA's are statistically significant. The major reason for prolonged hospitalization in the stent group was the prevention of subacute reclosure with intensive anti-coagulation therapy and the treatment of this complication. The major reason for more repeat intervention in the stent group was the occurrence of subacute reclosure.
Prolonged hospitalization and more repeat intervention resulted in significantly higher costs per patient in the stent group. At the end of 3 months follow-up the median costs per patient were $6,790 US Dollars (range $5,790 - $22,450) in the perfusion balloon group and $11,790 US Dollars (range $5,790 - $37,415) in the stent group (P < 0.005).

Currently, there is no evidence that 'the price that is to be paid' with prolonged hospitalization and more repeat intervention for subacute reclosure after bail out stenting translates into a long term gain in the sense of less restenosis and repeat ischemia during follow-up. As mentioned above, we were unable to detect a statistically significant difference in event free survival and angiographic restenosis after perfusion balloon angioplasty or stent implantation for acute or threatened closure. Lincoff and co-workers matched 61 patients who were treated with the Gianturco-Roubin® stent for acute or threatened closure with 61 patients who had received conventional therapy (thrombolysis, prolonged standard balloon inflation or perfusion balloon inflation). They could not detect any additional benefit from stent implantation (13). Additionally, it remains difficult to identify lesions that are best treated with perfusion balloons and lesions that are best treated with stents. We were unable to detect any significant difference in clinical and angiographic characteristics between the patients who were treated with a perfusion balloon and those who received a stent. Stent implantation generally results in a more rapid restoration of normal coronary blood flow than perfusion balloon angioplasty. Therefore, stent implantation may be preferable in the setting of cardiogenic shock. However, in our population, we were unable to detect an increased use of stent implantation in those patients who were in shock. In the perfusion balloon group 2 (3%) patients were in shock versus 2 (5%) patients in the stent group (difference not significant). A prospective randomized comparison of perfusion balloon angioplasty versus stent implantation seems warranted to guide treatment choices for acute or threatened closure.

In chapters 7 and 8 we report our initial clinical experience with the active perfusion system described previously, during elective coronary angioplasty.

In chapter 7 we report our experience with the system in 2 patients undergoing high risk PTCA. In a third patient we compared standard balloon inflation with subsequent prolonged inflation supported by the active perfusion system.

Several factors have been identified as being associated with a high risk of death and hemodynamic collapse during PTCA balloon inflation. In a retrospective study, Ellis et al. evaluated 8,052 PTCA procedures (14). They found that left ventricular failure due to vessel closure at the dilatation site was the most common cause of death. Left ventricular failure was independently correlated with female sex, an area of myocardium at risk > 50% and PTCA of a proximal lesion in the right coronary artery (14). Bergelson and co-workers published a prospective study in 61 patients, in whom risk factors associated with hemodynamic coll-
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lapse were evaluated (15). They found that an area of myocardium at risk > 50%, a left ventricular ejection fraction < 35%, multivessel disease and diffuse disease in the coronary artery undergoing dilatation, were independent predictors of risk for hemodynamic compromise. Additionally, the risk for hemodynamic collapse increased when a patient presented with several of these characteristics (15). The first 2 patients described in chapter 7 had several risk factors for hemodynamic collapse during balloon inflation. In the first patient a lesion in the left main coronary artery was dilated. Therefore, the area of myocardium at risk was > 50%. Additionally, there was multivessel disease. The second patient had an area of myocardium at risk > 50%, 3 vessel disease and an ejection fraction of 35%. Both patients were treated primarily with the active perfusion system, because they were considered to be at high risk for hemodynamic collapse during standard PTCA. They both had an adequate PTCA result.

The third patient underwent angioplasty during a study comparing standard PTCA with active perfusion angioplasty. There was pronounced ST-segment elevation and hemodynamic collapse after 1 min. of standard balloon inflation. During subsequent inflation with support of the active perfusion system, the electrocardiogram revealed only slight abnormalities and the blood pressure remained normal.

Active perfusion during angioplasty may have contributed to the reduction of myocardial ischemia during the second inflation in this patient. However, myocardial adaptation to ischemia induced by the first inflation may also have contributed to a reduction of ischemia during the second inflation. Several authors have demonstrated that a single episode of ischemia as short as 3 minutes is sufficient to induce adaptive metabolic changes that protect the myocardium from the effects of a subsequent prolonged inflation (16,17). This mechanism has been called preconditioning. However, the standard inflation in this patient lasted only 1 min. which on the basis of animal studies is too short to trigger preconditioning (16). A more likely explanation for a protective effect of the first inflation seems to be the opening of collateral vessels in response to the first inflation (16,18). This change in collateral support to the ischemic area has been demonstrated by Cribier and colleagues. They injected contrast medium into the right and left coronary arteries during balloon inflation in a proximal lesion in the left anterior descending coronary artery (18). One way to account for the protective effect of the first inflation is to perform a third standard inflation of the same duration as the first inflation. The omission of a third inflation is a shortcoming in the protocol comparing standard PTCA to active perfusion PTCA with prolonged inflation in the same patient.

Chapter 8 reports the initial results of a randomized comparison of standard balloon angioplasty and active perfusion angioplasty with 10 min. balloon inflation. This study was part of a multicenter study comparing both PTCA modalities.
This multicenter study is to test the hypothesis that prolonged balloon inflation improves the primary angioplasty result and reduces restenosis. Primary endpoints of the multicenter study are initial PTCA result, clinical events during 6 months follow-up and 6 months angiographic restenosis. We reported the patients who were included in this study at our center, because their data provide additional insight into the efficacy and safety of the active perfusion system during elective angioplasty.

Eleven patients were randomized to standard angioplasty and 14 patients were to undergo active perfusion angioplasty with 10 min. uninterrupted balloon inflation. There were no statistically significant differences regarding the clinical characteristics of both groups. Ischemia was compared in both groups with the aid of an angina pectoris score and 12 lead electrocardiograms. The specially designed PTCA catheter was unable to cross the lesion in 3 patients randomized to active perfusion angioplasty. They underwent subsequent successful standard PTCA. The time until the occurrence of maximum angina was significantly longer in the active perfusion group. The number of electrocardiographic leads showing ST-segment elevation was significantly lower in the active perfusion group and the maximum sum of ST-segment elevation was significantly less in this group. In all active perfusion patients the balloon inflation could be maintained for 10 min. in the active perfusion group 1 patient underwent emergency surgery for acute closure. There was procedural success in all other patients.

In the perfusion group there was prolonged spasm after PTCA in 2 patients. It only subsided after 2 intracoronary injections of 200 μg of nitroglycerin. This spasm may be indicative of vessel wall trauma by the jet exiting the active perfusion catheter. Grill et al. have reported indirect clinical evidence that active hemoperfusion causes trauma distal to the catheter tip (19). Four patients who underwent active perfusion of the right coronary artery with the system evaluated in this thesis, developed high grade atrioventricular block (19). None developed heart block during the preceding standard inflation and heart block disappeared upon reduction of the flow rate only to recur with increased flow. The authors speculate that the vagally mediated Bezold-Jarisch reflex may be initiated by arterial stretch secondary to a 'jet effect' on the arterial wall. An alternative explanation may be ischemia induced by coronary artery spasm secondary to a 'jet effect'.

There are also indications of damage to the vessel wall by a 'jet effect' from animal experiments. McDonald and colleagues report animal experiments with an active coronary perfusion system, that revealed histopathologic evidence for 'jet lesions' in the vessel wall (20). In a series of pig experiments, they perfused the left anterior descending coronary artery at flow rates up to 21 ml/min. Histopathologic examination revealed absent endothelium distal to the catheter tip in all animals. The elastica interna showed focal injuries in 3 cases. In our own
animal experiments, mentioned previously, 1 animal died secondary to ventricular fibrillation at the end of 20 min. perfusion at 60 ml/min. in the left anterior descending coronary artery. Flow measurement with a clamp-on doppler flow probe showed no flow in the artery distal to the angioplasty site. Upon macroscopic examination, there was a hemorrhagic infarction involving the anterior wall distal to the PTCA site and the intraventricular septum. Sixty ml/min. clearly represents over perfusion of the left anterior descending coronary artery (20). Nevertheless, in a subsequent experiment with 20 ml/min. flow, there was a hematoma in the vessel wall distal to the catheter tip. In control experiments with standard inflation macroscopic and microscopic examination never revealed any vessel wall damage distal to the PTCA site. A flow rate of 20 ml/min. is within the normal range for left anterior descending coronary artery flow in pigs (20).