The effect of fracture on femoral head blood flow

Osteonecrosis and revascularization studied in miniature swine

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Miniature swine were used to study the effect of cervical fracture on femoral head blood flow. Laser Doppler flowmetry was used to evaluate femoral head blood flow before and after the fracture, after internal fixation with or without compression, and 8 weeks post-fracture. Fluorescent bone-labeling was performed at 2, 4 and 6 weeks post-fracture. Femoral head blood flow decreased to 40 percent of baseline following fracture, partly from the disruption of venous drainage. Histologically, all femoral heads showed some degree of trabecular thinning, microfracture, and neovascularization when compared with controls. Analyses of the laser Doppler flowmetry data, fluorescent label histology, microradiography and bone densitometry indicated that late (4–6 weeks) revascularization produces severe trabecular mechanical weakening and resultant femoral head collapse. Femoral head ischemia following fracture probably falls along a continuum, with only the more severe cases proceeding to mechanical collapse.

Femoral neck fractures in the minipig produce femoral head necrosis of a severity and incidence which closely parallels that of the human population; thus, the minipig is a useful model for further study of complications following femoral neck fracture in humans.

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We describe a model for femoral neck fracture in the miniature swine and report the effect of femoral neck fracture, reduction, and internal fixation on femoral head blood flow.

Material and methods

The swine is considered to have proximal femoral vascular anatomy most similar to that of the human (Ghoshal and Getty 1968, Salter 1983). Gottinger miniature swine were selected because they are smaller (therefore somewhat easier to handle), and they undergo physeal closure at a smaller size (50–70 kg) than normal swine. 10 miniature swine weighing 43–68 kg were used for the study; 5 had closed upper femoral epiphysis and 5 had not. The pigs were premedicated with azaperon (1 mg/kg), atropine sulfate (0.025 mg/kg), and ketamine (20 mg/kg), intubated and placed on a 1% halothane, 40% oxygen mix. A posterior tibial arterial line was inserted into the left leg for continuous monitoring of the arterial pressure. After a betadine scrub, an anterolateral approach was made to the right hip joint and proximal femur. A pin was placed in the ilium and in the midshaft femur, and a distractor was used to displace the femoral head from the acetabulum 2–3 mm to enable the surgeon to visualize the location of the screw for insertion. The hip was not dislocated during the procedure. A specially designed hollow screw with internal and external threads (Figure 1) was inserted into the superior acetabulum. Teflon shrink tubing was attached to the screw head and an internal screw with teflon leader was used to seal the hole within the screw. An endoscopic 2.2-mm flexible laser Doppler probe was passed into the teflon tube, hollow screw and, after anterior capsulotomy to confirm the placement of the probe against the femoral head, femoral head blood flow was determined. The Periflux Pf1 Laser Doppler Flowmeter (Perimed, Stockholm, Sweden) was used for all measurements. Articular cartilage has no moving blood cells and does not impede penetration of the 2 mW He-Ne laser light into the subchondral bone (Swiontkowski et al. 1986). Doppler flowmetry was used to measure femoral head blood flow before and after a femoral neck fracture was created, and after internal fixation. Additionally, varus and valgus reductions were made and femoral head blood flow recorded prior to the anatomic reduction and internal

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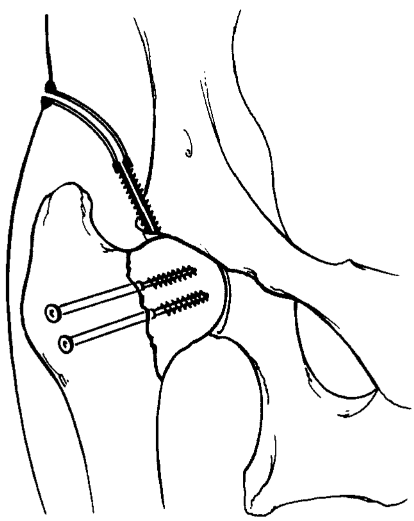


Figure 1. The hollow acetabular screw inserted into the superior acetabulum which allows the flexible 2.2-mm laser Doppler flowmetry probe to be placed against the femoral head.

fixation to assess the effect of malreduction on femoral head blood flow (Smith 1959). Laser Doppler flowmetry assesses blood cell motion at a depth of 3.5 mm in cartilage-covered trabecular bone (Notzli et al. 1989). For each measurement site, 2 periods of data collection of 4 minutes in duration at 5 second intervals were utilized. Blood cell flux (BCF) and direct current levels were recorded for each site. BCF is proportional to total red cell motion (Nilsson et al. 1980). The direct current level is inversely proportional to the amount of light returning to the photodetectors (Nilsson et al. 1980). If venous stasis is produced, the direct current level declines. In this way, arterial lesions (decreased blood cell flux, increased direct current) can be differentiated from venous lesions (decreased blood cell flux, decreased direct current).

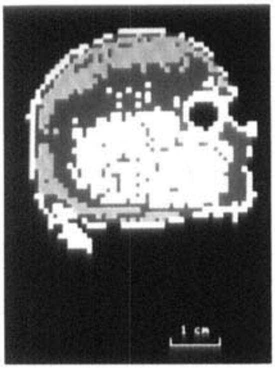
The fracture was created by scoring the superior, anterior and posterior femoral neck at the mid-femoral neck (measured halfway from the anterior intertrochanteric line to the margin of the articular cartilage), with a water-cooled oscillating saw and completing the fracture with an osteotome. The 10 pigs were divided into 3 groups; Control Group A, Kirschner wire no-compression Group B, and screw compression Group C. We wished to study the worst-case effect of no contact between the fracture fragments as a control group; and therefore in Group A which consisted of 2 swine, a 0.4-mm thick silastic sheet (Dow Corning) was trimmed to the size of the femoral neck and interposed between the fracture fragments. Two 2.0-mm Kirschner wires were placed across the fracture through the silastic sheet to stabilize the fracture. The fracture occurred distal to the physis in the juvenile animals (Figure 4). This method was selected for the control group as we could not leave the animal with an unfixed fracture. In Groups B and C, which were composed of 4 swine each, the fractures were fixed with 2.0-mm Kirschner wire fixation and 4.0-mm cancellous screw fixation, respectively. The juvenile and adult animals were divided equally into the 3 groups; 1 in the control group, 2 in the K-wire group, and 2 in the screw group. Following the third flowmetry measurement, the acetabular screw was sealed, and the end of the teflon tube with the silastic filler was tunneled under the skin and left beneath the skin in the superior gluteal region. The screw assembly was checked to ensure that it could be opened and resealed from the subcutaneous end and that the flexible flowmetry probe could be passed into the hip joint prior to wound closure. This system was designed to allow interim blood flow measurements without opening the surgical site. The swine were returned to their pens postoperatively and were seen to convert from a 3-pointed to a 4-pointed gait on the third or fourth postoperative day. One of the control swines maintained a 3-point gait throughout the 8-week course of the experiment.

3 separate fluorescent bone labeling compounds were administered orally, in 3 doses each, to the animals over the experimental period as a method of assessing bone remodeling. Xylenol Orange at 200 mg/kg was given over Weeks 2 and 3, Calcein Green 50 mg/kg over Weeks 4 and 5, and Oxytetracycline 50 mg/kg over Weeks 6 and 7. Interim femoral head laser Doppler flowmetry measurements were attempted at Week 3 under ketamine (20 mg/kg) anesthesia.

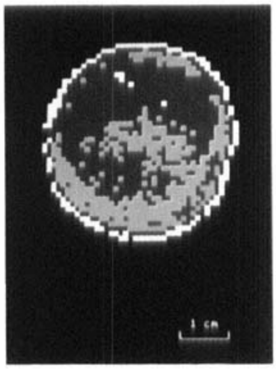
Arterial blood pressure remained stable throughout each of the procedures. There were no operative or perioperative complications and all animals survived throughout the entire 8-week experimental period. Teflon tube and silastic insert loosening precluded interim measurement in 8 of the 10 animals. Of these, 6 animals (1 Group A, 3 Group B, 2 Group C) developed loosening of the screw implant from the acetabulum. In 2 animals (1 Group A, 1 Group C), the tube was removed due to the development of wound infection thought to be related to the stiffness of the silastic filler which produced erosion of the skin. In the 2 remaining animals, femoral head blood flow was assessed at 21 and 35 days postoperatively, respectively (Figure 5). In 7 animals the femoral neck fracture healed uneventfully (Figure 4). In the control Group nonunion occurred in 1 animal, and in the other animal healing occurred around the perimeter of the femoral neck. In Group B, 1 malunion occurred due to backing out of the K-wires.

The animals were killed at 8 weeks with a barbiturate overdose. Prior to death, under a ketamine anes-

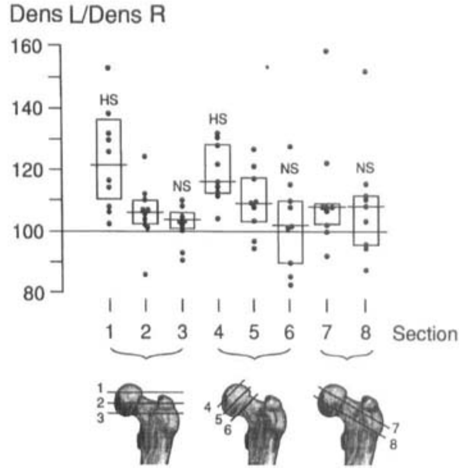
Figure 2. Representative sections utilized with Isotom single density photometry.



Experimental side.

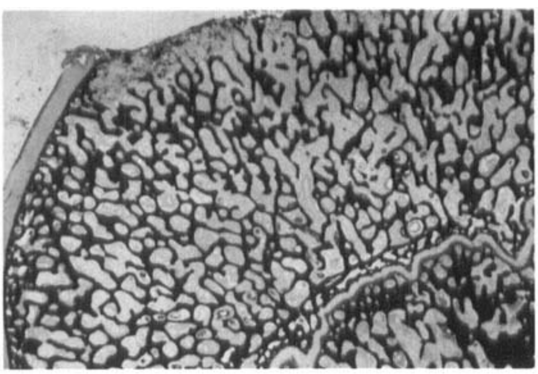


Control side.

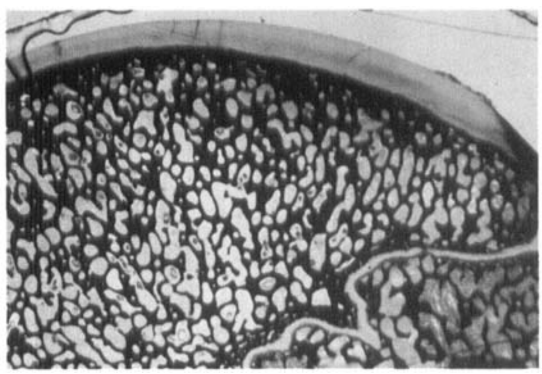


Normalized data (experimental/control) for Isotom single density photometry for each of 8 different CT sections examined.

Figure 6. Giemsa stain from animal number 10.

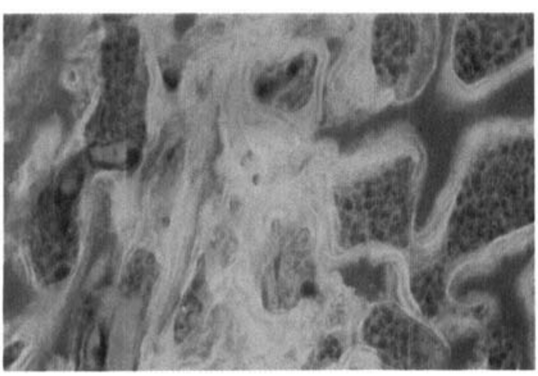


Experimental side.

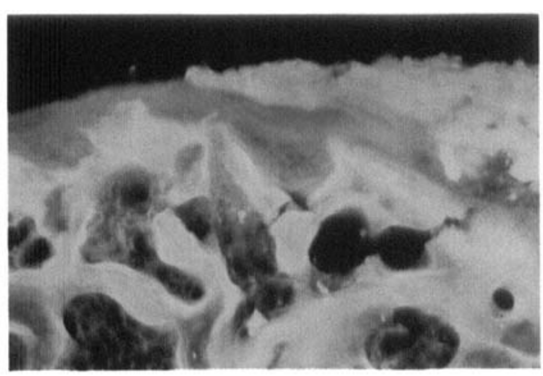


Control side.

Figure 7. Fluorescent microscopy.



Representative section from collapsed femoral head showing only the yellow tetracycline label.



Representative section from structurally sound femoral head showing the presence of all three labels, indicating early revascularization.

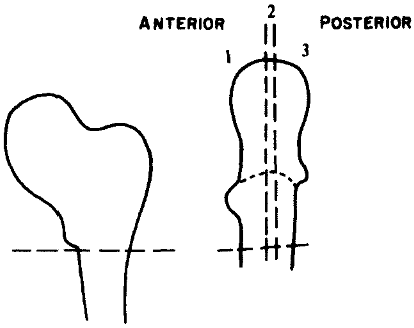
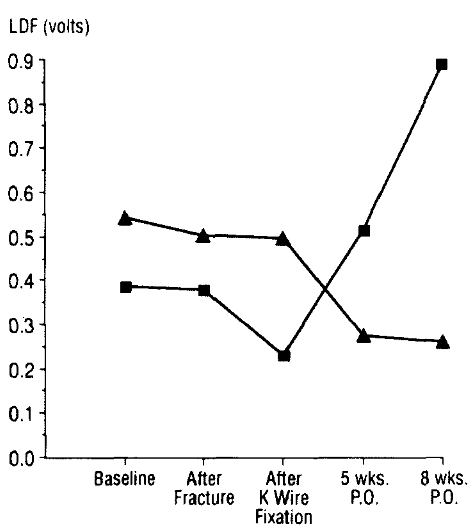


Figure 3. Partition of proximal femora for microradiography and histologic evaluation.

Figure 4. Experimental (right) versus control (left) radiographs from pig number 10.

thetic, femoral head blood flow measurement was successfully completed by a limited approach to the hip joint through the old incision or through the intact tube-screw system. Disulphine Blue at 62 mg/kg was administered intravenously prior to the barbiturate for qualitative assessment of bone perfusion.

Both femora were harvested, stripped of all soft tissues, and frozen at –70 °C. Bone density assessment of both femora was performed using the Isotom (Elasser and Ruegsegger 1976, Institute for Biomedical Technology, Zürich) single photon CT scanner (Figure 2). In this system an I^{125} source is used with 80 percent of the x-rays at about 27 KeV. Beam-hardening is corrected for. The bone is scanned through 49 different angles; the intensity of the beam is thereby measured 128 times per scan. The reconstruction yields a 128-by-128 matrix at local linear absorption coefficients. Graphic software (Graphic ITOMO; P. Weber, MEM Institute, Berne) allows graphic reconstruction without distortion in a VAX 11-730 microcomputer, and histograms of density are produced. Whole bone radiographs were made, and the femoral head and neck were cut sagittally into 2 fragments (Figure 3).



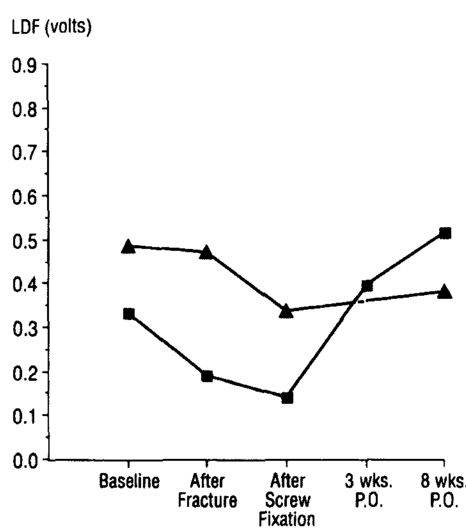


Figure 5. Complete laser Doppler flowmetry data of an animal that developed femoral head collapse (left) and one that did not (right). ■ Blood cell flux, ▲ DC level.

Table 1. Femoral head blood flow following fracture. Values expressed in millivolts, *SD*

	Baseline	After fracture	After fixation	8 weeks
Blood cell flux	451 *64*	171 *41*	226 *31*	381 *61*
DC level	490 *14*	414 *4*	419 *5*	342 *12*

Table 2. Internal fixation technique. Values for blood cell flux in millivolts, *SD*

	Baseline	After fracture	After fixation	8 weeks
A–Control, n 2	368 *21*	150 *26*	61 *19*	225 *42*
B–K-wires, n 4	397 *63*	173 *52*	237 *37*	372 *59*
C–Screws, n 4	547 *78*	179 *36*	296 *31*	452 *71*

Table 3. Effect of skeletal maturity on femoral head blood flow following femoral neck fracture. Values for blood cell flux in millivolts, *SD*

	Baseline	After fracture	After fixation	8 weeks
Adult, n 5	558 *79*	173 *56*	290 *37*	227 *52*
Juvenile, n 5	344 *45*	169 *17*	161 *25*	522 *66*

The anterior fragment was further divided for microradiography and 100 micron sectioning, and the posterior fragment was decalcified and sectioned (60 micron) for Giemsa, Hematoxylin and Eosin, and von Gieson's staining for histologic assessment.

Doppler flowmetry data were stored at collection on a PDP 11/03 computer and analyzed for average, maximum and minimum values and standard deviations. Bone density data were analyzed by comparing representative single photon CT cuts from operated on (right) versus control (left) femora (Figure 2). Statistical analysis of flowmetry and density data was performed using ANOVA. Individual cuts were represented in pictorial form by assigning colors to individual density ranges (Figure 2). The percentage of the section in each density range was directly compared to the control section. As a qualitative control, the microradiographs were visually compared for density. Disulphine blue perfusion sections and thin stained sections were evaluated with standard light microscopy. Representative sections from each experimental and control side were examined using fluorescent microscopy, and the presence or absence of each of the 3 labels was recorded (Figure 7). The presence of oxytetracycline alone was interpreted as late revascularization, oxytetracycline and calcein green as intermediate revascularization, and all 3 markers as early revascularization.

Results

Laser Doppler flowmetry

The fracture reduced the femoral head blood flow in all animals (Table 1). The fracture also produced a decline in femoral head DC level which implies that at least part of the effect occurred on the venous side; impaired venous drainage produces blood cell pooling which results in more light absorption and hence a lower direct current level. Neither valgus (390 mV vs 313 mV in valgus) nor varus malreduction produced a further decline in femoral head blood flow, and, in fact, varus malreduction (262 mV vs 389 mV) produced a trend toward higher femoral head blood flow. Internal fixation did not alter femoral head blood flow, and although there were no differences between the 3 experimental groups, there was a tendency for the cancellous compression screw group to produce greater improvement in femoral head blood flow, relative to the post-fracture value (Table 2). The only differences between the adult and juvenile animals were: a) an improvement in femoral head blood flow following internal fixation (non-technique dependent) for skeletally mature animals, and b) a higher femoral blood flow at 8 weeks for juveniles (Table 3). Femoral head blood flow was higher at death ($P > 0.005$) in those animals (7 of 10) that developed gross femoral head collapse. Both of the silastic interposition animals were included in this group. Complete flowmetry data from 1 animal that developed gross femoral head collapse and 1 that did not are depicted in Figure 5. These animals were the only 2 where a functioning silastic tube was available for an intermediate assessment, the others having been removed for loosening or wound breakdown.

Bone density, fluorescent and light microscopy data

All operated (right) femoral heads had lower density than the control sides. This was most dramatic in those animals which developed gross femoral head collapse. The 2 animals with silastic interposition developed the highest degree of bone resorption. The CT data confirmed this impression, as densities were lower for the experimental side in all 10 animals where the CT cuts included the femoral head (Figure 2). Light microscopy showed trabecular thinning, fracture and the appearance of increased numbers of thicker walled arterioles that was proportional to the amount of femoral head deformity (Figure 6). Fluorescent microscopy revealed the presence of all 3 labels indicative of early revascularization in those femoral heads (3 of 10) that did not develop gross collapse, and the presence of only oxytetracycline in 5 of the 7 femoral heads with collapse (Figure 7). This corresponds to later (beyond the fourth week) revascularization.

Discussion

Disruption of the blood supply to the femoral head has been well accepted as the cause of post-traumatic osteonecrosis. Arteriographic studies have added to our knowledge in this area by defining the vascular anatomy of the proximal femur and demonstrating disruption of the arterioles following femoral neck fracture (Trueta 1953, 1957, Claffey 1960). There have been no studies demonstrating the direct effect of femoral neck fracture on femoral head blood flow, probably due to the lack of an easy-to-use, reliable mechanism for the real-time measurement of bone blood flow. However, Strömqvist (1983) has demonstrated by Tc-MDP scintigraphy in patients that femoral head blood flow as reflected by osteoblastic uptake of Tc-MDP is adversely effected.

Controversy exists as to the effect of emergent reduction, capsulotomy, and internal fixation with compression on the eventual development of post-traumatic osteonecrosis of the femoral head (Boitzy 1980, Drake and Meyers 1984, Swiontkowski et al. 1986). Although its clinical role in the development of osteonecrosis of the femoral head is subject to dispute (Drake and Meyers 1984), intracapsular tamponade has been shown to have a negative effect on femoral head blood flow at pressure levels equivalent to local (femoral head) venous pressures in animal models (Ganz et al. 1981, Swiontkowski et al. 1986, Woodhouse 1962). Pressures in these ranges have been documented in 10–15 percent of patients with femoral neck fracture (Soto-Holl et al. 1963, Drake and Meyers 1984); capsulotomy should therefore be considered as a therapeutic option. Strömqvist (1983) and Strömqvist et al. (1988) have documented that decompression improves femoral head circulation. In order to define the effect of reduction and internal fixation on femoral head blood flow and the ultimate incidence of osteonecrosis, this minipig femoral neck fracture model was developed.

Laser Doppler flowmetry has been shown to be an easy-to-use, accurate method of assessing bone blood flow (Hellem et al. 1983, Tothill 1984, Swiontkowski et al. 1986). The method cannot distinguish physiologic perfusion from bleeding, but by assessing subchondral blood flow of the femoral head across the articular cartilage, this limitation is avoided. The flexible 2.2-mm flowmetry probe allowed measurement through flexible tubes, but technical problems limited the interim measurements to 2 animals.

Our experiment supports the following hypothesis. Femoral neck fracture results in arteriolar disruption and distortion of venous drainage channels. This produces a relative femoral head ischemia, as documented by laser Doppler flowmetry. The degree of disruption of these vascular channels is directly related to the decrease in femoral head blood flow. Reduction and, more importantly, internal fixation produce improvement in femoral head blood flow and limit the degree of ischemia to some extent. There is a suggestion that internal fixation with compression may improve the blood flow, but this was not significant in this small group of animals. The response to ischemia is a gradual improvement in femoral head blood flow to normal by vascular dilatation and neovascularization (Strömqvist 1983). This was documented by histologic studies showing that all femoral heads, regardless of whether collapse had occurred, showed trabecular thinning and neovascularization. If the ischemic period is prolonged, the hyperemic response is delayed and increased, producing more dramatic trabecular thinning, resorption of dead bone, neovascularization, and ultimate collapse of the weight-bearing area of the femoral head. The time course of this schema was well documented by the fluorescent labels showing that the femoral heads which collapsed revealed the presence of only oxytetracycline along the remodelling trabeculae. This confirms the observation that revascularization occurred at an interval beyond the fourth week post-fracture.

Acknowledgements

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References

Boitzy A. Fractures of the proximal femur. In: Treatment of Fractures in Children and Adolescents (Eds. Weber, B. G, Brunner, C, Freuler, F.) Springer Verlag, Berlin 1980: 254–67.

Claffey T J. Avascular necrosis of the femoral head. An anatomical study. J Bone Joint Surg (Am) 1960; 42: 802–9.

Drake J K, Meyers M H. Intracapsular pressure and hemarthrosis following femoral neck fracture. Clin Orthop 1984; 182: 172–6.

Elasser U, Ruegsegger P. Frühzeitige quantitative Erfassung von veränderungen der Knochenmineralisation mittels Digitaltomographie. Biom Technick 1976; 21: 315.

Ghoshal N G, Getty R. Arterial blood supply to the appendages of the domestic pig (sus scrofa domesticus) Parts I and II. Iowa State J Science 1968; 43 (2): 125–52.

Hellem S, Jacobsson L S, Nilsson G E, Lewis D H. Measurement of microvascular blood flow in cancellous bone using laser Doppler flowmetry and 133Xe clearance. Int J Oral Surg 1983; 12 (3): 165–77.

Nilsson G E, Tenland T, Öberg P A. Evaluation of a laser Doppler flowmeter for measurement of tissue flow. IEEE Trans Biomed Eng 1980; BME-27, (10).

Notzli H P, Swiontkowski M F, Thaxter S T, Carpenter G K, Wyatt R. Laser Doppler flowmetry for bone blood flow measurements: helium neon laser light attenuation and depth of perfusion assessment. J Orthop Res 1989; 7 (3): 413–24.

Salter R B. Personal communications. 1983.

Sevitt S. Avascular necrosis and revascularization of the femoral head after intracapsular fractures A combined arteriographic and histological necropsy study. J Bone Joint Surg (Br) 1964; 46: 270–96.

Smith F B. Effects of rotatory and valgus malpositions on blood supply to the femoral head. Observations at arthroplasty. J Bone Joint Surg (Am) 1959; 41: 800–15.

Strömqvist B. Femoral head vitality after intracapsular hip fractures. 490 cases studied by intravital tetracycline labeling and Tc-MDP radionuclide imaging. Acta Orthop Scand (Suppl 200) 1983: 1–71.

Strömqvist B, Nilsson T, Egund N, Thorngren K-G, Wingstrand H. Intracapsular pressures in undisplaced fractures of the femoral neck. J Bone Joint Surg (Br) 1988; 70: 192–4.

Swiontkowski M F, Tepic S, Perren S M, Moor R, Ganz R, Rahn B A. Laser Doppler flowmetry for bone blood flow measurement: correlation with microsphere estimates and evaluation of the effect of intracapsular pressure on femoral head blood flow. J Orthop Res 1986; 4 (3): 362–71.

Swiontkowski M F, Winquist R A. Displaced hip fractures in children and adolescents (published erratum appears in J Trauma 1986 Dec; 26 (12): 1160). J Trauma 1986; 26 (4): 384–8.

Tothill P. Bone blood flow measurement. J Biomed Eng 1984; 6 (4): 251–6.

Trueta J. The normal vascular anatomy of the human femoral head during growth. J Bone Joint Surg (Br) 1957; 39: 358–94.