UTERO-PLACENTAL BLOOD FLOW IN HYPERTENSIVE PREGNANCY AND THE EFFECT OF NIFEDIPINE ADMINISTRATION

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PATIENT DATA

PATIENT NO.:	1
AGE: (YRS)	31
PARITY:	1
SMOKER:	No
GESTATIONAL AGE: (WKS)	36
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	10.3
PLATELET COUNT:	198
URIC ACID (m mol/L)	0.28
UREA (m mol/L)	3.6
CREATININE (m mol/L)	79

CHAPTER 1

ANATOMY OF PLACENTATION

(A) Lobular architecture

From end of first trimester the placenta attains its definitive architecture but continues to grow thereafter (Pangiel 1986).

It becomes divided into 15 - 30 lobules by septa divided by a combination of trophoblast and decidual elements.

To each lobular space there are 1 - 3 cotyledons which are the fetal placental units of the branched villous tree.

(B) Vascular Anatomy

The maternal and fetal blood streams are separated by a placental barrier. The fetal blood is contained in the placental villi and the maternal blood circulates in the intervillous space.

When the blastocyst implants, the endometrium is in the luteal phase and the spiral arteries lie immediately below the superficial capillary plexus.

Several days elapse before the invading trophoblast effects

free communication between the maternal arterial system and the developing intervillous space of the placenta. During this time the arteries become more coiled as a preparation for stretching out in the last trimester as the uterus expands. During this early period the arteries undergo a marked dilation. This progressive dilation (Brosens 1967) is achieved in two phases. In the first trimester there is a transmural colonisation of the distal spiral walls by trophoblast and the migration of trophoblast (cytotrophoblast) in the lumen of the arteries. The cells migrate down the inner walls of the arteries (a process likened to wax dripping down a candle) to almost the myometrial segments. Initially the vascular endothelium is involved then the media of the arteries becomes invaded by cytotrophoblast and finally the bulk of the musculo elastic tissue in the wall of the artery is replaced by fibrinoid tissue.

At 14 - 16 weeks there is a similar process of migration into the myometrial portion of the spiral arteries (second wave of trophoblastic migration) as far as their origin from the parent radial arteries.

This adaptive process has thus changed spiral arteries to utero-placental arteries and a low pressure, high conductance vascular system has been formed. (See Figure 1)

CHAPTER 2

PHYSIOLOGY OF UTEROPLACENTAL FLOW

REGULATION OF UTEROPLACENTAL FLOW

1. Maternal

The regulation of the utero-placental circulation appears to be under neuro-endocrine and environmental factors. Oestrogen increases uterine blood flow by vasodilation and adrenaline or noradrenaline infusions decrease utero-placental flow by vasospasm (Greiss 1967). Angiotensin II infusions have a vasodilatory effect in lower doses and in higher doses the uterine blood flow decreases (Leib 1980).

Maternal pyrexia (+ 1.5 deg C) has been associated with decreased utero-placental flow in pregnant ewes (Oakes 1976) and maternal exercise is associated with decreased uterine blood flow in several animal models (this may be due to catecholamine release or by pyrexia). Maternal cigarette smoking has been associated with decreased flow, possibly due to nicotine stimulation of catecholamine release. (Pirani 1978).

The question of autoregulation of the uteroplacental circulation has been studied in sheep (Greiss 1982) and it is postulated that these findings are similar in different mammalian species.

Autoregulation is defined as: "local tissue mechanisms which act intrinsically in blood vessels to control vascular resistance, excluding the effect of stimulation elsewhere by the body." In sheep the pregnant uterus approaching term demonstrates a linear pressure flow relationship with a slope approximating to 1. In humans there appears to be a differential reactivity of the myo-endometrial and placental components of total uterine blood flow (Kauppila 1980). There is evidence of autoregulation in the myo-endometrial arteries but in the utero placental vessels there is a passive widely dilated system. The changes in the vascular system of the uterus must thus be related to the stage of pregnancy and are dependent upon the extent of the so-called normal physiological changes particularly in the spiral arteries.

In early pregnancy the overall picture is similar to that of the non-pregnant state with only a small amount of blood directed to the placenta. The myometrial arteries have an amount of musculo-elastic tissue remaining and retain the ability to autoregulate. The adaptive process of trophoblastic invasion has not occurred to a sufficient

extent to alter the pattern of autoregulation seen in the uterus.

In late pregnancy there is 80-90% of the total uterine blood flow going towards the placenta with its widely dilated utero-placental arteries and therefore the overall picture is one of passive dilation (Greiss 1982).

The neurendocrine and humoral regulation referred to previously must be effected at the vascular tree proximal to the utero-placental arteries.

There is a large degree of reserve of placental function which can compensate for reduced placental blood flow without any impairment of fetal wellbeing. Separation of the placenta of up to 25% carries no untoward fetal effects (Fox 1978). In studies on hypoxic sheep and dogs it appears that there is an excess of oxygen diffusing capacity which normally exceeds fetal requirements (Power 1967, Lorijn 1980). It is postulated that this degree of excess capacity of placental function makes it unnecessary for the placenta to possess the ability to autoregulate its blood flow.

In labour uterine contractions result in decreased uterine venous outflow and arterial blood supply to the placenta. This is a function of the resting tone and the contraction amplitude and frequency (Harbert 1982). The blood flow in

the final hour of labour has been recorded as only 66% of the mean of the preceeding 48hr period. It appears that the placental reserve is sufficient to meet the requirements of the fetus in the short periods of decreased flow during contractions. During a contraction the venous outflow of the intervillous space is decreased and therefore the pool of blood in the intervillous space is not reduced thus there is a continued oxygen supply, although at a reduced level (Ramsay 1977).

It is obvious that if the frequency or amplitude of contractions exceeds a certain level in a placenta which has a decreased reserve then fetal distress will result.

Maternal posture has an effect on utero-placental flow, when compared to the supine position the left lateral position has been shown to increase utero-placental blood flow (Kauppila 1980).

2. Fetal

The umbilical blood flow derives from both ventricles in parallel which is directed at a largely passive umbilical bed. There is a high umbilical artery flow to the placental villi which is not responsive to changes in oxygen tension in the maternal side of the placenta. The umbilical artery flow is +/- 270mls/min at term which accounts for 57% of the fetal cardiac output and is acutely sensitive to oxygen

tension in the umbilical venous and arterial blood (Dawes 1969).

The fetal placental blood flow has been shown to be decreased in pregnancies complicated by intrauterine growth retardation (Laurin et al 1987). Dihydralazine, which crosses the placenta has been shown to increase the umbilical artery blood flow in hypertensive pregnancy (Jouppila et al 1985).

CHAPTER 3

THE EFFECT OF HYPERTENSION IN PREGNANCY ON UTEROPLACENTAL BLOOD FLOW

When the effect of hypertension on uteroplacental blood flow is studied it is important to distinguish between chronic hypertensive states and pre-eclampsia.

If pre-eclamptic pregnancies are studied, it is notable that placental blood flow is reduced (Dixon et al 1963 and Lunell et al 1984) although intra-uterine growth retardation is not a constant feature of pre-eclampsia (McGillivray et al 1981). McGillivray noted that IUGR is an associated feature in 21% of cases if proteinuric hypertension is present but when there is only hypertension present in the second half of pregnancy the birth weight distribution of the pregnancies is normal. Lunell's findings indicate a reduced placental blood flow in hypertensive patients, even when normotensive and hypertensive women who delivered normal weight infants were studied and women who delivered growth retarded infants were excluded. The mean reduction in placental blood flow was estimated at 50% from his radio-isotope studies using Indium 113 m accumulation curves. In addition to the presence of hypertension, the time of onset of the hypertension appears to be of note. In early onset pre-eclampsia the rate of IUGR is higher than the normal

(18.2%) but in late onset has been found to be less (5.6%) than the normal hospital incidence which was 8.6% (Long et al 1980) in that particular study.

If essential hypertension is studied a different disease pattern is encountered. Essential hypertension in early pregnancy may be associated with IUGR but many women with this disease deliver babies of a normal size (Arias 1975).

In view of the defective placentation (discussed in the next section) which occurs in pre-eclamptic pregnancies before 20 weeks, it is difficult to understand why the occurrence of growth retardation is not present in all cases of pre-eclampsia. Similarly, it is still unclear why pre-eclampsia may only become clinically evident in the third trimester when the pathology of the placental vessels is present long before. It may be possible that the hypertension of pre-eclampsia is an adaptation to enable greater blood flow to the placenta.

It has been found that the presence of IUGR appears to correlate well with the degree of plasma volume expansion rather than the degree of hypertension (Arias 1975). Plasma volume expansion is a feature of normal pregnancy (Hytten FE 1963) and a failure of this expansion is associated with IUGR in chronic hypertensive women. If there is appropriate volume expansion, then these women will deliver babies which

are appropriately grown. Gallery (1979) and Soffronoff (1977) found an inverse correlation between the degree of hypertension and the plasma volume expansion but in contrast to Arias did not find an overall reduction in plasma volume in known chronic hypertensive women.

It is clear that in both pre-eclamptic and chronic hypertensive pregnancy there is a reduction in plasma volume and in pre-eclamptic pregnancy a reduction in utero-placental blood flow. It is postulated that utero-placental blood flow is reduced in chronic hypertensives on account of the higher incidence of IUGR.

CHAPTER 4

DEFECTIVE PLACENTATION IN PRE-ECLAMPTIC PREGNANCY

The changes in anatomy of the spiral arteries in the first 16 weeks of pregnancy have been described in Section 1. When pregnancies with pre-clampsia are studied it appears that the second wave of trophoblastic invasion of the spiral arteries (which occurs from 12 - 16 weeks) is absent.

The progressive loss of musculo-elastic tissue in the media of the spiral arteries of the utero-placental bed do not extend beyond the deciduo-myometrial junction and do not penetrate to the radial arteries as they do in a normal pregnancy (Robertson WB et al 1975). (Figure 2)

The haemodynaemic consequences of this constricted segment is that placental blood flow is reduced. In addition, the segment of the utero-placental artery is responsive to vasomotor influences and therefore, conceivably, may be dilated by antihypertensive agents which could act at this site.

The histology of these segments (Robertson et al 1975) indicate a specific pathological entity. With the study of placental bed biopsies and also caesarean hysterectomy

specimens it has been found that the proximal segments of these arteries (in common with the basal arteries and spiral arteries of the decidua parietalis) is involved with the lesion termed "acute atherosis". (Figure 3).

By definition, acute atherosis involves lipid changes in smooth muscle cells, necrosis of smooth muscle, fibrinous vasculosis and infiltration of the damaged wall by macrophages.

It follows that acute atherosis can only be present in the walls of arteries with smooth muscle present and therefore cannot be a feature of normal utero-placental arteries which have undergone replacement of their muscular wall with fibrinoid material.

Robertson likens the pathological features of acute atherosis to the early stages of atheroma, namely, the accumulation of lipid in smooth muscle cells or myointimal cells which eventually perish freeing their lipid to be taken up by macrophages. The question why atherosis is the pathological feature of the arteries in hypertensive pregnancy and not the arterionecrosis of systemic accelerated essential hypertension has not been assessed to date.

It is notable that similar changes have been described in pregnancies complicated by intrauterine growth retardation without hypertension (Khong et al 1986).

The reason for the failure of the second wave of trophoblastic invasion and the development of a pathological spiral (placental) artery in pre-eclamptic pregnancy is not clear. It would be of immense use to the clinician involved with the treatment of pre-eclampsia if a compound which could preferentially dilate the constricted segments of the uteroplacental arteries and improve blood flow to the placenta was available.

CHAPTER 5

THE INVESTIGATION OF UTERO-PLACENTAL BLOOD FLOW WITH RADIO-ISOTOPE ACCUMULATION/DISAPPEARNCE STUDIES

There have been a number of methods of investigation used in respect of the utero-placental blood flow. The investigation of this area is difficult as there are a number of different arteries supplying the uterus, the placenta is not at a constant site and its size varies according to gestational age and between patients. The presence of a fetus has also proved a hinderance and a number of methods of investigation are applicable to animal experimentation only.

In human subjects the study of utero-placental blood flow has frequently been undertaken with radioisotope studies.

Initially disappearance studies of locally injected isotopes were used. Radioactive 24Na was used by Brown et al 1953 and Dixon et al 1963 who injected the isotope through the abdominal wall into the choriodecidual space and analysed its disappearance curve. The method provided the initial data to suggest that utero-placental blood flow is reduced in hypertensive pregnancy. This method was criticised as the size of the blood pool into which the sodium was

injected was unknown, the isotope binds to the tissue and the sodium recirculates thus distorting the disappearance curve. The second two disadvantages have been overcome with the use of ^{133}Xe, it does not bind to the tissues and is excreted via the lungs. This method was used by Lippert et al 1973 and permits examination of utero-placental blood flow at very low dosages.

A simpler method with greater accuracy has been developed using the rate of accumulation (and not disappearance) into the placenta. If the isotope is injected intravenously and its rate of accumulation into the placenta is analysed a reproducable determination of utero-placental flow is obtained. Accumulation studies have been more frequently performed recently and the isotopes used have been ^{133}Xe, Indium 113m, Technetium 99m.

Rekonen et al 1976 described an intravenous technique using ^{133}Xe. The isotope was injected intravenously and the patient held her breath for 20 seconds immediately afterwards. Accumulation curves in the placenta were studied and an estimation of intervillous and myometrial flow obtained. This technique has provided information on dihydralazine (Jouppila et al 1985) which does not decrease intervillous flow when given by an intravenous infusion. Kauppila et al 1980, demonstrated a decreased intervillous flow in the supine compared to the left lateral position by

this method. In addition, Kauppila could not demonstrate any change in myometrial blood flow and postulated that the myometrial blood flow but not the intervillous flow is under autoregulation influences.

The techniques of using Indium 113m and Technetium 99m are most widely used now as they permit examination of utero-placental blood flow at acceptable doses of radiation (Van der Merwe EJ et al 1970).

The isotopes are bound to albumin or red cells in the case of Technetium or to transferrin with Indium, thus there is minimal transfer across the placenta to the fetal circulation. Most authors have used the blood flow index (described in Chapter 7.10) to analyse the blood flow to the placenta. This variable allows analysis between different patients and within the same patient.

In addition there are a number of different methods of analysis of the time-activity curves and it has been possible to assess the myometrial and placental components of the time-activity curves (Lunell N O et al 1979). Following this differential analysis of the two components of utero-placental blood flow an index of the intervillous perfusion has been calculated (Bodis et al 1985) in addition to the blood flow index. Bodis found that the intervillous perfusion index was prolonged in growth retarded pregnancy

before the blood flow index was reduced.

Using intravenous accumulation studies hydralazine (Lunell et al 1983) has been found not to decrease utero-placental blood flow or vascular resistance. Pindolol (Lunell et al 1984) when used in therapeutic doses does not alter utero-placental blood flow. Labetolol (Lunell et al 1984(b)) has been shown by this method not to decrease utero-placental blood flow in hypertensive pregnancies.

The original work of Brown et al 1953 which demonstrated the reduced blood flow in pre-eclampsia has been confirmed by the newer methods. (Lunell et al 1984(b), Philipp et al 1986).

As indicated above there has not been an antihypertensive which has increased utero-placental blood flow in pre-eclamptic pregnancy.

CHAPTER 6

THE ROLE OF NIFEDIPINE IN THE TREATMENT OF HYPERTENSION IN PREGNANCY

Nifedipine is an antagonist of the calcium influx through the slow channel of the cell membrane. Nifedipine is an effective anti-hypertensive agent with minimal side-effects and well tolerated. Its place in hypertensive therapy in non-pregnant patients is not clearly defined (Frishman WH 1984) but it is finding an increasing place in the treatment of hypertension in Groote Schuur Hospital. It is useful in both long-term and emergency treatment.

Given sublingually it has an onset of action in 5 - 10 minutes (Erbel et al 1983) and has few side effects. The effect of the nifedipine in lowering the BP appears to be proportional to the magnitude of the pretreatment BP (Frishman WH 1984). The drug is safe and an excessive hypotensive action is not a feature of its clinical use (Haft JI 1984).

Additional advantages of the action of nifedipine are that cardiac output is maintained or increased and there may be a preferential vasodilatation of cerebral vessels (Payen et al

1984). This property may be beneficial in eclamptic pregnancy when cerebral ischaemia has been postulated as a cause of brain damage (Richards et al 1986) and an increase in cerebral perfusion may be protective.

Nifedipine has also been found to cause a decrease in platelet aggregation (Dale et al 1983) which may be mediated by calcium transport across the platelet membrane. It has also been postulated that platelet adhesion is a factor in the reduced blood flow to the placenta and the vasoconstriction which is seen in pre-eclamptic pregnancy (Wallenburg et al 1986).

Nifedipine has been reported to be successful in treating the hypertension of pre-eclampsia (Walters BNJ 1984) and its further investigation is indicated.

Studies in pregnant goats indicate that nifedipine has no detrimental effect on utero-placental blood flow (Veille et al 1986) and in vitro studies on umbilical artery preparations raise the possibility of a beneficial effect of nifedipine in lowering the fetal placental vascular resistance (Margard et al 1984).

The introduction of an antihypertensive drug which can be given orally (sublingually) with rapid control of blood pressure but without severe hypotension is a major advance

in treatment of hypertension in pregnancy. Cases of severe hypertension can be managed without invasive monitoring and the same drug can be used for maintenance therapy. In view of its efficacy and safety the further investigation of nifedipine in the treatment of hypertension in pregnancy and particularly its effect on utero-placental blood flow is essential.

CHAPTER 7

THE INVESTIGATION OF THE EFFECT OF NIFEDIPINE ON UTERO-PLACENTAL BLOOD FLOW

In view of the finding of decreased blood flow to the placenta as a major patho-physiological feature of pre-eclampsia and the efficacy of nifedipine in controlling the hypertension of pre-eclampsia, a study of the effect of nifedipine on utero-placental blood flow in hypertensive pregnancy was undertaken. It would be necessary to establish that a new antihypertensive agent should be able to maintain, if not increase utero-placental blood flow before it gained acceptance in the treatment of antenatal cases.

The aims of the study were three fold:

1. To validate the indium 113m radio-isotope accumulation method and to assess its value as a measure of utero-placental blood flow.

2. To measure the utero-placental flow before and after nifedipine administration.

3. To investigate the antihypertensive effect of nifedipine under controlled conditions in pregnant hypertensive patients.

The outline of the study was as follows:

1. Selection of Patients

(A) Pregnancy duration greater than 28 weeks.

(B) Anterior placentae or placentae with a large anterior component which was located by ultrasound.

(C) Singleton pregnancy.

(D) No evidence of fetal compromise as indicated on cardiotocographic monitoring.

(E) Mean maternal diastolic blood pressure equal to or greater than 100mgHg in the day before the study.

Patients were excluded if

(A) They had received any anti-hypertensive medication in the previous 48 hours before the study.

(B) The patients had received magnesium sulphate therapy.

(C) The patient was in labour or experienced any uterine contractions.

2. Consent

Written consent was obtained from each patient.

3. Ethical Safeguards

The study was approved by the University of Cape Town Ethics and Research Committee and by the Radiation Protection Officer of Groote Schuur Hospital, Cape Town.

The total dose of Indium was 3mCu (111 mBq) per patient (1 mCu per study).

The total body radiation dose for the mother was 51 mR. The dose to the fetal blood is 24 mR (Van der Merwe 1970) which is well within the limit of radiation to a pregnant woman of 500mR (International Committee of Radiological Protection, Publication 26).

4. Preparation of Radio-isotopes

Indium 113m was prepared from its parent isotope by eluting the isotope with HCL in accordance with the manufacturers instructions.

The radioactivity of the eluate was checked so that the sample for injection contained 1mCu (37mBq).

5. Calibration of the gamma camera

An Elscint 410 gamma camera with a medium energy parallel hole collimator was used. The area under study was outlined using a cobalt marker. The collimator was then positioned as closely as possible to the area of the placenta, with the patient positioned as described below.

6. Positioning of patient

The patient was positioned supine on the examining table

with a 30^{o} lateral tilt with the placenta positioned uppermost. On the lowermost arm a Space Labs automatic blood pressure recorder was placed and a recording of systolic blood pressure, diastolic and mean arterial pressure and pulse rate was measured every 5 minutes. In the uppermost arm an intravenous cannula was inserted and attached to a 50cc vacolitre of 4.2% NaCl and run slowly. The patient was supported by pillows and rested at ease throughout the measurements. The patient was asked not to move during the study. The collimator was placed as closely as possible to the anterior abdominal wall.

7. Technique of recording the accumulation curves

The Indium 1mCi was injected directly into the intravenous cannula over a period of 3 - 5 seconds. The inflow tubing was sealed by way of a valve before the Indium injection. After the injection the valve was opened and saline allowed to run into the antecubital fossa. The gamma camera recorded the accumulation of radioactivity under the collimator continuously for 480 seconds. This accumulation curve was stored on magnetic tape. All subsequent recordings were made in a similar fashion apart from a correction for background radiation made at the beginning. Three recordings were made on each patient. Two baseline recordings at times 0 and 30 min. and one after the administration of the drug at time 60 min.

8. Administration of the Nifedipine

Nifedipine 5mg (Adalat, Bayer Pharmaceuticals) was given after the second baseline recording at time 30 min. The Nifedipine was administered sublingually and the patient instructed to bite the capsule and chew the remainder. She was then given a mouthful of water and instructed to swallow the empty capsule. The same procedure was followed with the administration of the placebo capsule. The placebo was a mixture of vitamins in a gelatin capsule.

9. Randomised selection of patients into Nifedipine or placebo groups

Initially the patients were given a number at booking into the antenatal clinical. The last digit of this number was used to randomise the patients into Nifedipine or placebo groups. A patient with an odd last digit was given a placebo and a patient with an even last digit was given Nifedipine.

10. Analysis of Data

The time activity curves were stored on magnetic tapes and each curve was analysed at a later time. Each curve was analysed separately but the method of analysis was identical.

Initially the final radio-isotope picture was studied and the area of the placenta outlined with a graphic pen.

Secondly, summed images at 10 second intervals were analysed and the number of counts in the placental area plotted against the time in a manner similar to the specimen in diagram Figure 4.

After the time activity curve has been plotted two parameters were calculated:

1. The maximum count rate (MCR) which is determined from the highest plateau level of the curve.

2. The rise time RT which is the time taken to rise from T5 (the time at 5% of the maximum count rate) to T95 (the time at 95% of the maximum count rate).

3. The blood flow index (BFI) is determined from the formula:

$$\text{Blood Flow Index} = \frac{\text{Maximum Count Rate}}{\text{Rise Time}}$$

$$\text{BFI} = \frac{\text{MCR}}{\text{RT}}$$

Thus three values of the blood flow index (BFI) are calculated for each patient, two before and one after the administration of the drug.

The blood flow index is a measure of utero-placental blood flow. The maximum count rate gives an indication of the

size of the blood pool in the placenta and the rise time indicates the time taken to achieve a steady state of influx and eflux of blood into the placental pool. A fast rise time indicates either; a small placenta, a rapid blood influx into the placenta or a combination of the two conditions. By using a ration of the maximum count rate and rise time a correction is made for the size of the placental pool. Thus the utero-placental blood flow index is a measure of the rate of influx of blood into the placenta.

CHAPTER 8

RESULTS

1. MATERNAL CHARACTERISTICS

The two groups of patients are described in Table 1. There were 9 patients in each group. There were no significant difference between the two groups.

2. BLOOD PRESSURE

The effect of Nifedipine and placebo on blood pressure in each patient is shown in Table 2. The mean change in blood pressure i.e. the difference between the BP measurements after the administration of Nifedipine or placebo are shown in a bar diagram with the standard deviations (Figure 5). The Nifedipine group showed a marked decrease in the systolic, diastolic and mean arterial pressure and an increased pulse rate when compared to the placebo group.

3. BLOOD FLOW INDEX

The individual estimations of maximum count rate (MCR), rise time (RT) and blood flow index (BFI) is shown in Table 3. When plotted on a bar diagram with the standard deviations (Figure 6) the outward similarity between the three estimations is notable.

When the BFI from the first two estimations are plotted as in Figure 7 the correlation co-efficient can be calculated and reproducibility of our technique analysed.

STATISTICAL ANALYSIS

1. Blood Pressure

When the Nifedipine and placebo groups were analysed, the differences between the pre- and post-treatment pulse and blood pressure recordings were significant. A reduction in systolic ($p < 0.02$) diastolic ($p < 0.01$) mean arterial pressure ($p < 0.02$) and a rise in the pulse rate ($p < 0.005$) was seen in the Nifedipine group.

The student's T-test was used for the analysis.

2. Blood Flow Index

(A) A correlation co-efficient between the utero-placental blood flow index of the first and second scans is 0.90 (Figure 7).

(B) There is no significant difference between the blood flow indices; mean count rate, rise time and utero-placental blood flow index when the before and after parameters were analysed in the placebo and Nifedipine groups.

The analysis of variance was used.

SIDE-EFFECTS

One patient in the Nifedipine group complained of a headache, otherwise there were no specific side-effects.

Patient Number 5 in the Nifedipine group experienced progressive discomfort from a full bladder. She could not be moved because of the constant position needed by the study. The discomfort may explain the rise in blood pressure after Nifedipine administration.

The rise in the mean blood pressure seen in the control group may be due to anxiety and mild fatigue. The cause of the anxiety and fatigue is possibly that the patient were unable to move for over one hour whilst the study was being performed.

CHAPTER 9

DISCUSSION

The study of Nifedipine on utero placental blood flow will be discussed with reference to the three stated aims of the study (Chapter 7 p.23).

The first aim was to validate the Indium 113m radio-isotope accumulation method and to assess its value as a measure of utero-placental blood flow. From Fig. 7 it can be seen that there is a close correlation between the two studies which were performed before the administration of the Nifedipine or placebo. The correlation coefficient was 0.90. This indicates that the utero-placental blood flow index is a consistent determination of utero-placental blood flow in the conditions present in our study.

The studies of Husslein (1985) who used a similar method of investigation also found a constant utero-placental blood flow in a placebo treated group of patients. Occasional difficulties were encountered in the calculation of the utero-placental blood flow index due to the irregular appearance of the time activity curves (eg. patients 5 and 7 in the placebo group). The nature of the curves suggest that there was a uterine contraction during the study. These curves were analysed by taking the maximum value to be

that obtained before the onset of the contraction. The reason why a ratio of the rise time and maximum count rate was used as the measure of utero-placental flow is as follows: The ratio takes into account the difference in size of the placentae in different patients. Thus a short rise time would indicate either a rapid blood flow into the placenta or a small placenta with average blood flow. By using the blood flow index the size of the placental blood pool is taken into account, and a value is obtained which can be used for inter patient or intrapatient estimations of blood flow.

The second aim of the study was to investigate the effect of Nifedipine on utero-placental blood flow. As outlined in Chapter 5, the utero-placental blood flow is reduced in hypertensive pregnancy (Brown 1953, Dixon 1963, Lunell 1984(b)) and any drug used to treat pregnant hypertensives should achieve blood pressure control in the mother without detrimental effects on utero-placental blood flow. The ideal drug for use in pregnancy would have a beneficial effect on utero-placental blood flow and increase it to normal levels. This could be achieved by a vasodilator agent which preferentially dilates the utero-placental vessels over the systemic vaculature causing a concomitant decrease in maternal blood pressure and increase in utero-placental blood flow. In view of Nifedipine's effectiveness in lowering the maternal blood pressure (Walters 1984) the

investigation of the utero-placental flow is necessary before it can be recommended for use in antepartum cases. Our results suggest that following the administration of Nifedipine there is a relative uterine vasodilation and a relative decrease in uterine vascular resistance which is proportional to the fall in blood pressure. Nifedipine does not appear to have a preferential effect however on uterine vascular resistance or to preferentially increase utero-placental blood flow.

This is the first study of the effect of Nifedipine on utero-placental blood flow but previous studies referred to in Chapter 5 have not found any hypotensive agent which increases utero-placental blood flow. Hydralazine (Lunell 1983) Pindolol (Lunell 1984), Labetolol (Lunell 1984(b)) and Prostacyclin (Husslein 1985) have all been investigated but found not to increase (or decrease) utero-placental blood flow. In view of these findings Nifedipine may have a place to play in both the emergency and maintenance treatment of pregnant hypertensives.

The third aim of the study was to investigate the use of Nifedipine in the acute situation under controlled conditions. As the results indicate, Nifedipine, in a 5mg sublingual dose caused a rapid fall in materal systolic, diastolic and mean arterial pressure which is significant when compared to a control group.

It was a notable finding that a rise in blood pressure was seen in the control group under resting conditions. The fact that the patients were not able to move possibly made them progressively more uncomfortable over the course of the study and thus elevated the blood pressure.

In the Nifedipine group one patient (number 5) experienced a slight rise in blood pressure after Nifedipine. This patient was feeling discomfort from a full bladder and could not be moved, thus it is felt that Nifedipine was not given a chance to be effective.

The absence of side-effects in the Nifedipine patients was notable, only one patient complained of a mild headache.

Nifedipine is suited to the emergency treatment of hypertensive episodes for a number of reasons:

1. The blood pressure is lowered in relation to the magnitude of the pre-treatment blood pressure.

2. Cardiac output is maintained.

3. Cardiac stimulation precipitating angina or myocardial infarction is rarely seen.

For these reasons blood pressure control can be undertaken without invasive monitoring of the patient (Frishman 1984).

CHAPTER 10

CONCLUSIONS

Nifedipine, in a 5mg sublingual acute administration, causes a significant fall in the systolic, diastolic and mean arterial pressure in a mixed group of pregnant hypertensives. A concurrent, significant rise in the pulse rate was seen.

The utero-placental blood flow index, which is a measure of utero-placental blood flow, was not significantly reduced following the administration of Nifedipine or a placebo. The utero-placental blood flow index was found to be a consistent measure of utero-placental blood flow in resting patients.

In the absence of serious side-effects it can be concluded that Nifedipine is a safe therapy in the acute treatment of hypertensive states in pregnancy.

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Finally, I would like to acknowledge the support, advice and enthusiasm of Professor D A Davey under who's guidance this project had been undertaken.

TABLE 1

MATERNAL AND FETAL CHARACTERISTICS OF THE NIFEDIPINE AND CONTROL GROUPS OF PATIENTS

	NIFEDIPINE n = 9	CONTROL n = 9
Mean Age (yr)	27.2	28.6
Proteinuria (Number of patients)	5	3
Median Parity	2 (0-5)	0 (0-4)
Mean Gestational age (yr)	35.8	34.7
Mean Birth Weight (gm)	2313	2894
Mean Birth Weight Percentile (%)	14.1	26.4
Mean Placental size (gm)	486	550

TABLE 2

A COMPARISON OF BLOOD PRESSURE RECORDINGS BEFORE AND AFTER THE SUBLINGUAL ADMINISTRATION OF NIFEDIPINE 5 mg OR A PLACEBO

	BEFORE				AFTER			
NIFEDIPINE	S	D	M	P	S	D	M	P
PATIENT 1	151	96	114	84	145	89	105	81
2	141	97	116	90	119	83	96	96
3	155	100	115	105	153	102	112	119
4	141	98	113	87	140	94	108	105
5	150	99	116	78	155	103	121	95
6	158	109	123	85	156	106	123	93
7	154	113	127	87	150	105	120	107
8	149	107	120	63	133	99	110	85
9	138	98	110	78	128	91	101	81
MEAN	148.6	101.9	117.1	84.1	142.1	96.9	110.7	95.8
PLACEBO								
PATIENT 1	160	99	115	78	175	99	108	83
2	167	114	130	111	177	119	132	110
3	147	97	115	88	140	93	112	75
4	143	89	105	83	141	93	104	80
5	168	110	127	76	169	113	130	80
6	154	111	125	80	150	110	125	86
7	147	94	112	98	152	98	117	90
8	138	98	109	85	140	102	114	88
9	128	92	103	80	128	96	104	73
MEAN	150.2	100.4	113.9	86.6	152.4	102.6	116.2	85

S = Systolic Blood Pressure (mm Hg)
D = Diastolic Blood Pressure (mm Hg)
M = Mean Arterial Pressure (mm Hg)

TABLE 3

INDICES OF UTERO PLACENTAL BLOOD FLOW

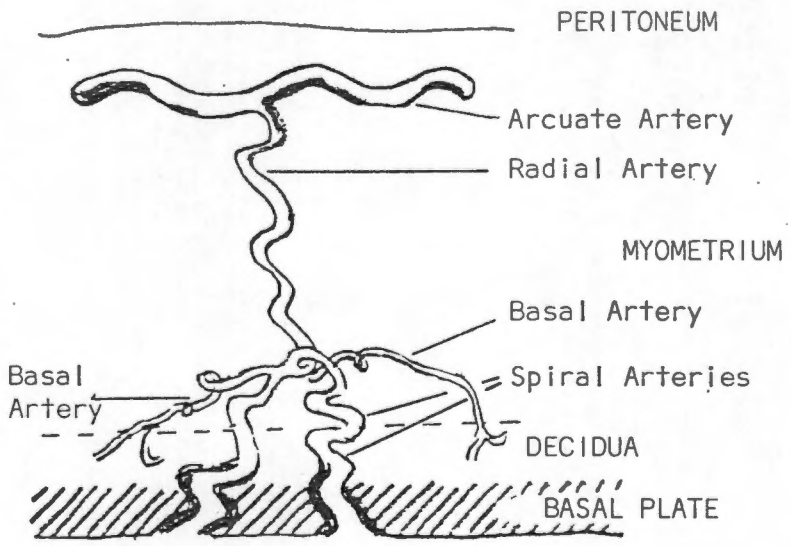
	1. PRETREATMENT			2.PRETREATMENT			3. 23 MIN. POST DRUG		
NIFEDIPINE	MCR	RT	BFI	MCR	RT	BFI	MCR	RT	BFI
1	300	47	6.4	320	47	6.8	300	64	4.7
2	120	71	1.7	155	140	1.1	165	121	1.4
3	380	115	3.3	340	68	5	470	103	4.6
4	290	51	5.7	330	60	5.5	340	86	4
5	130	44	3.0	100	60	1.7	185	75	2.5
6	270	120	2.3	250	102	2.5	360	99	3.6
7	205	70	2.9	195	51	3.8	225	70	3.2
8	140	150	0.9	185	144	1.3	180	92	2.0
9	120	74	1.6	125	68	1.8	205	112	1.8
MEAN	217.2	82.4	3.1	222.2	82.2	3.3	220	91.3	3.1
CONTROL									
1	210	66	3.2	270	86	3.1	135	140	1
2	180	34	5.3	175	42	4.2	170	114	1.5
3	165	70	2.4	175	82	2.1	175	79	2.2
4	160	78	2.1	140	48	2.9	210	114	1.8
5	175	70	2.5	170	83	2.0	210	79	2.7
6	225	97	2.3	-	-	-	350	112	3.1
7	190	122	1.7	155	139	1.1	205	73	2.8
8	160	82	2	185	75	2.5	205	69	3
9	340	49	6.9	300	50	6	410	50	8.1
MEAN	200.6	74.2	3.2	196.3	75.6	3.0	228.9	92.2	2.9

MCR = Maximum count rate (counts/10 sec)

RT = Rise time (sec)

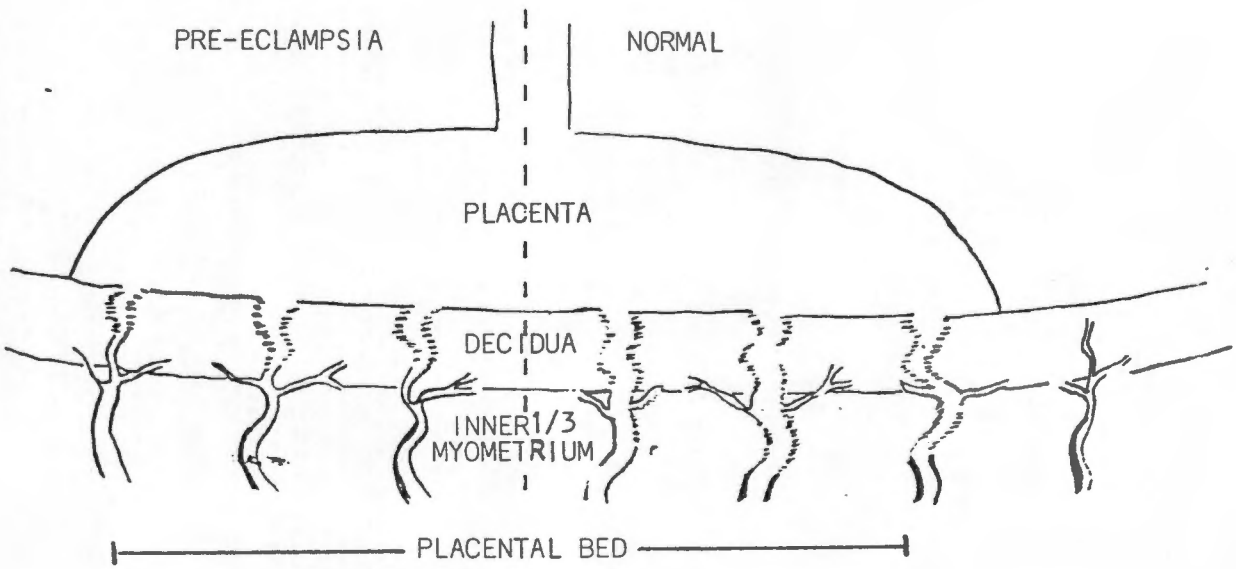
BFI = Blood flow index (counts/sec)

FIG. 1



DIAGRAMMATIC REPRESENTATION OF THE FULLY DEVELOPED BLOOD SUPPLY TO THE INTERVILLOUS SPACE.

FIG. 2



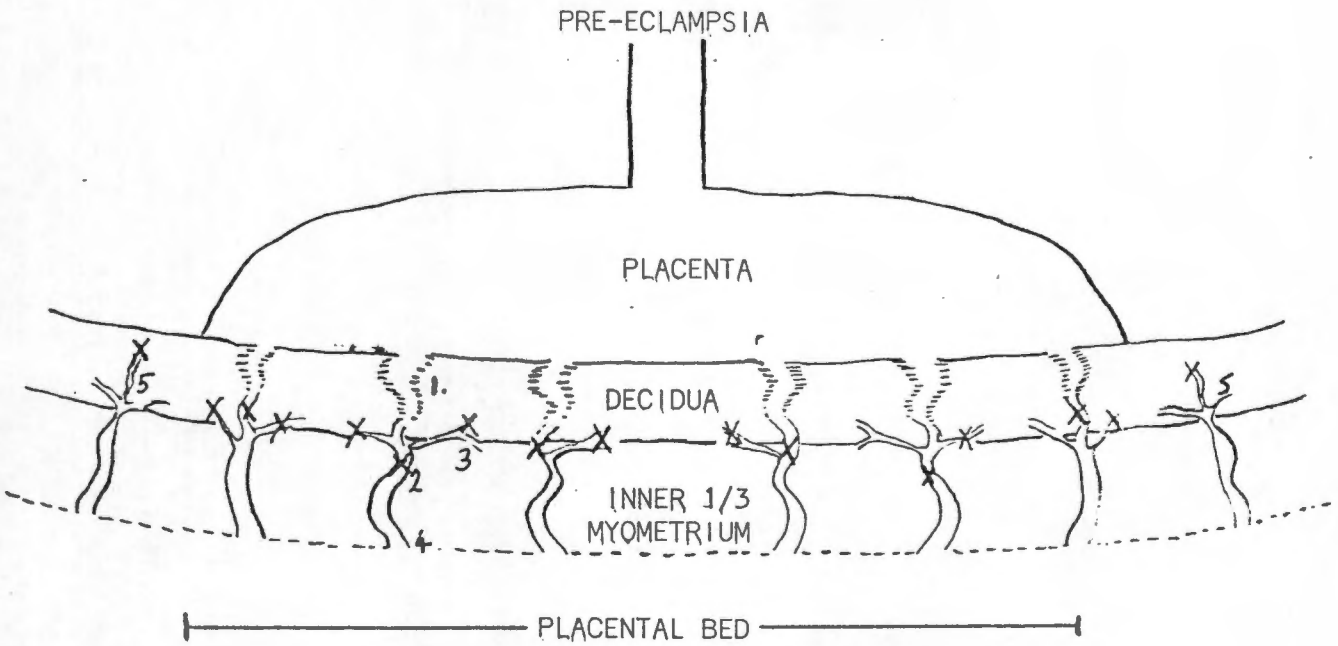
1. Spiral artery
2. Myometrial spiral artery
3. Basal arteriole
4. Radial artery
5. Non-placental bed spiral artery

Physiological changes

// Musculo-elastic structure

COMPARSION OF THE UTEROPLACENTAL BLOOD SUPPLY BETWEEN NORMAL AND PRE-ECLAMPTIC PREGNANCIES.

FIG. 3



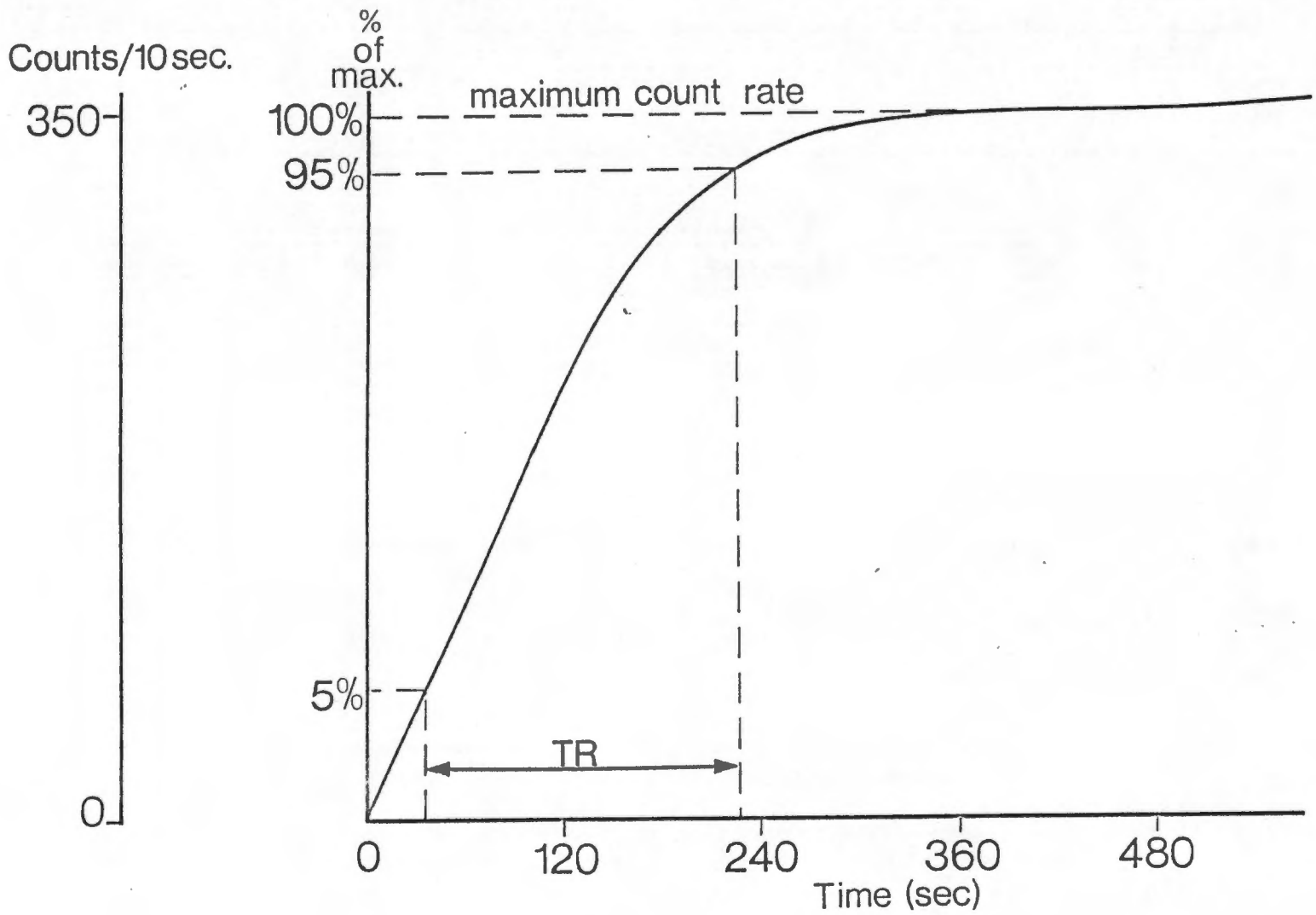
1. Spiral artery
2. Myometrial spiral artery
3. Basal arteriole
4. Radial artery
5. Non-placental bed spiral artery

Physiological changes
// Musculo-elastic structure
X Acute atherosis

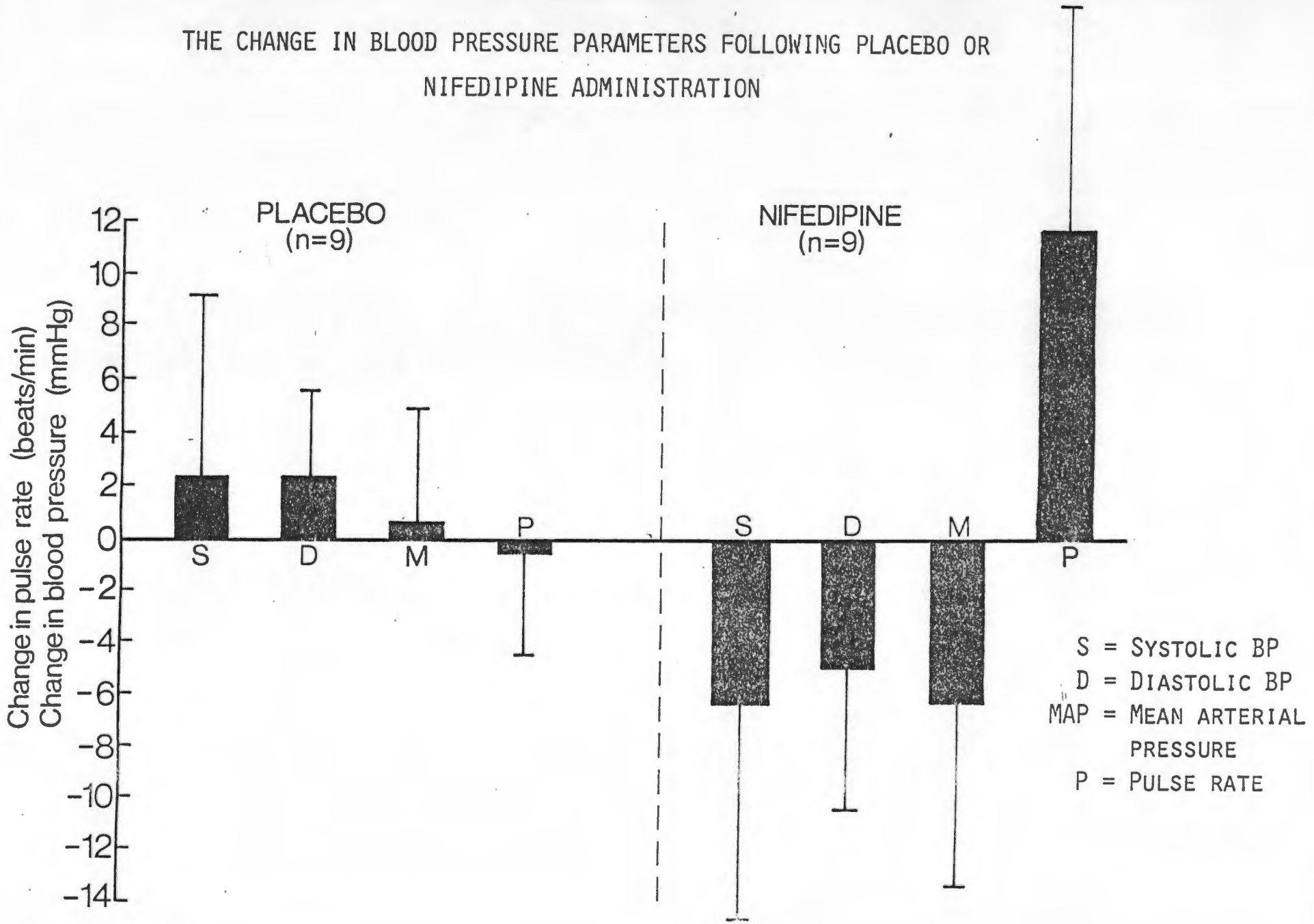
PATTERN OF DISTRIBUTION OF ACTUE ATHEROSIS (X) IN PRE-ECLAMPSIA.

FIG. 4

TIME-ACTIVITY CURVE FOLLOWING INDIUM 113M ADMINISTRATION



THE CHANGE IN BLOOD PRESSURE PARAMETERS FOLLOWING PLACEBO OR NIFEDIPINE ADMINISTRATION



A COMPARISON OF THE BLOOD FLOW INDEX IN 3 SEPARATE STUDIES
IN 2 GROUPS OF PATIENTS (± STANDARD DEVIATION)

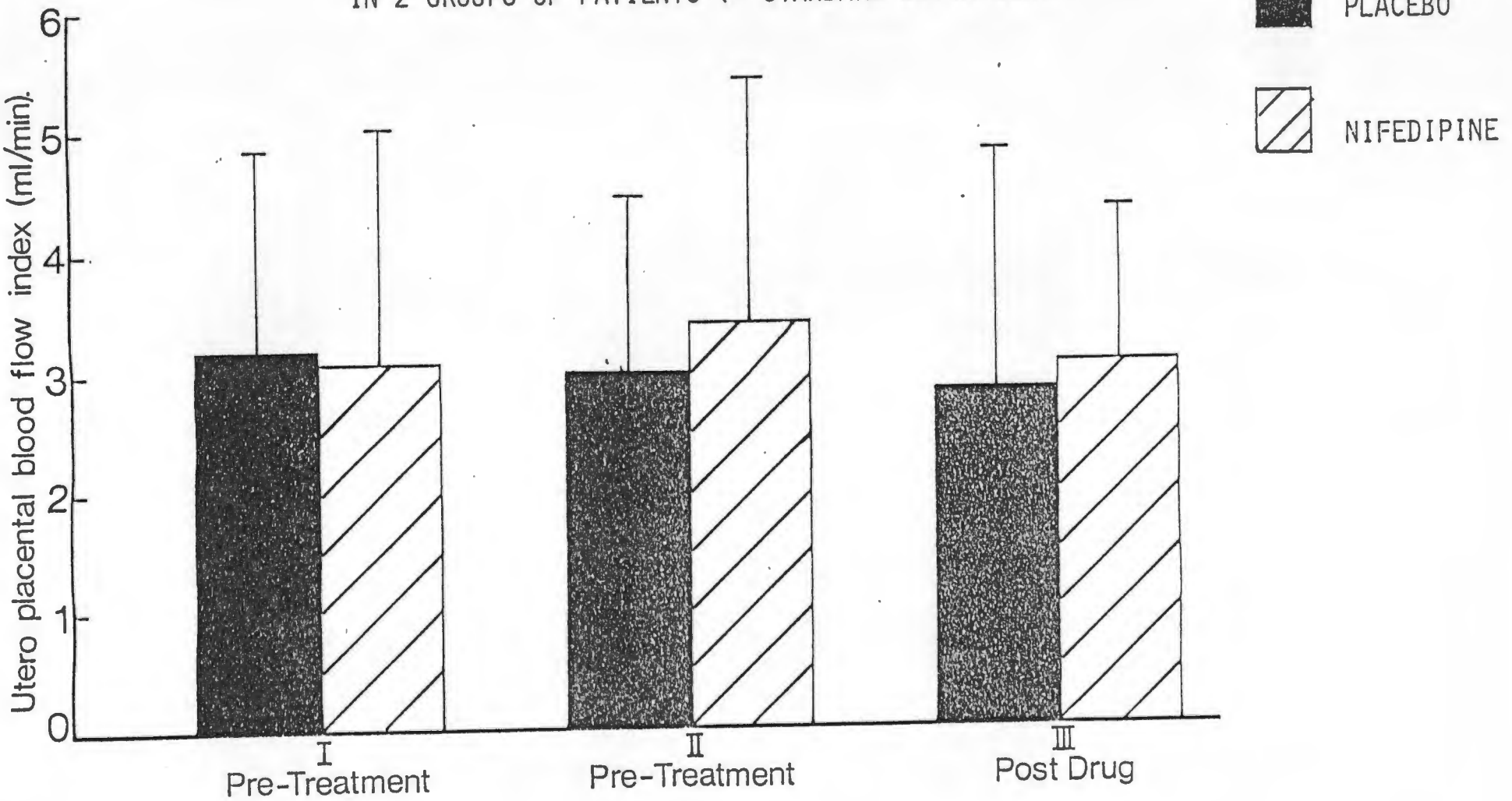
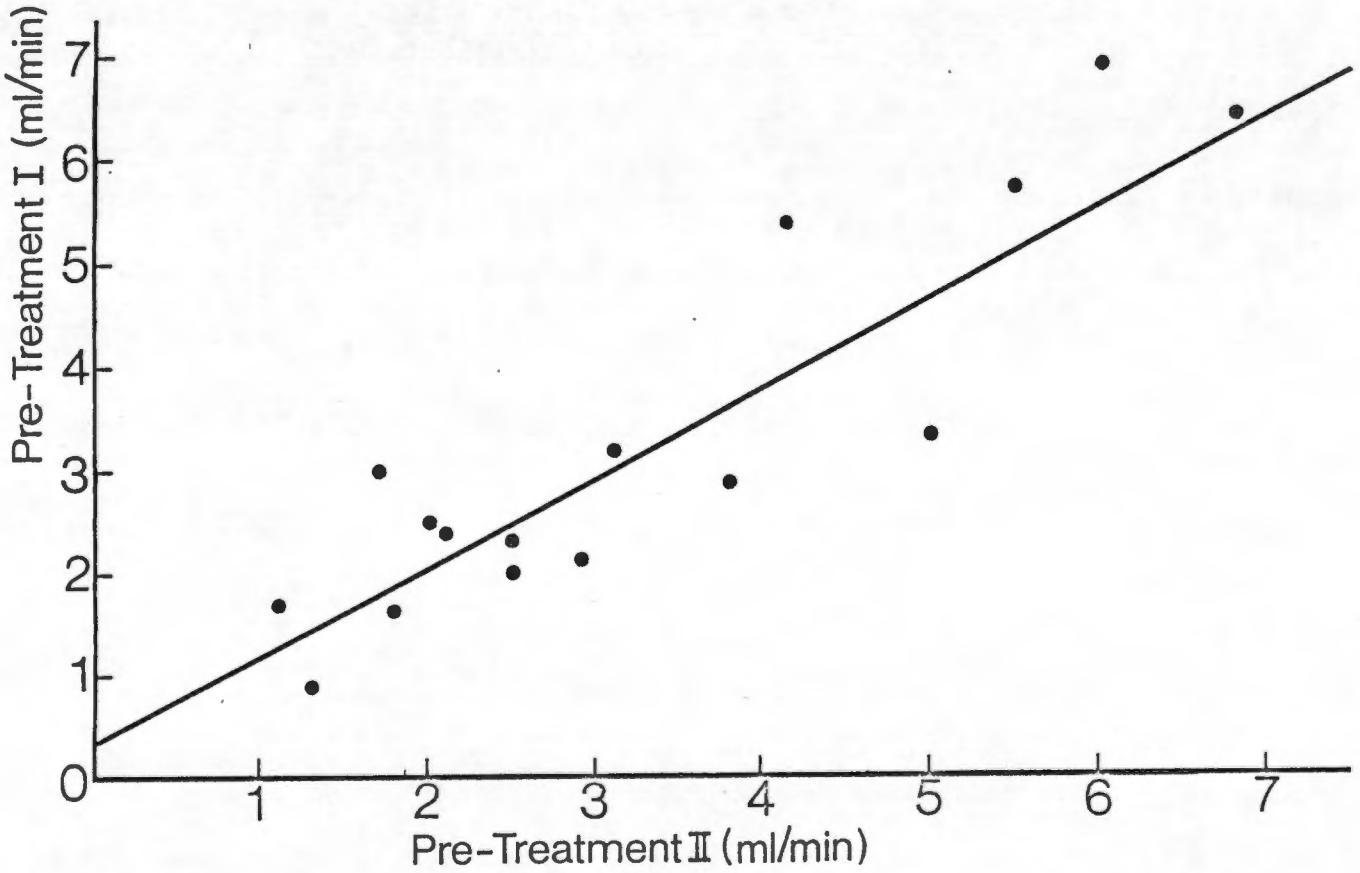


FIG. 7

A COMPARISON OF THE BLOOD FLOW INDEX IN 2 SEPARATE STUDIES IN THE SAME PATIENTS



PATIENTS TREATED WITH PLACEBO

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	160
	Diastolic	99
	Mean arterial pressure	115
Mean post-treatment blood pressure:	Systolic	175
	Diastolic	99
	Mean arterial pressure	108
Mean pre-treatment pulse rate		78
Mean post-treatment pulse rate		83

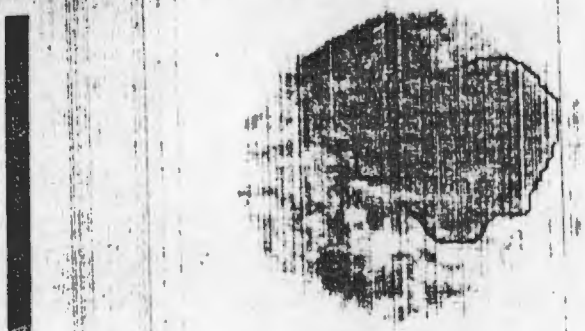
2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	210
	Rise time	66
	Blood flow index	3.2
Pretreatment scan II	Maximum count rate	270
	Rise time	86
	Blood flow index	3.1
Post-treatment Scan	Maximum count rate	135
	Rise time	140
	Blood flow index	1

JOHNSTONE,R 86/3225 68313 691

#49 SUMMED IMAGES:1-48

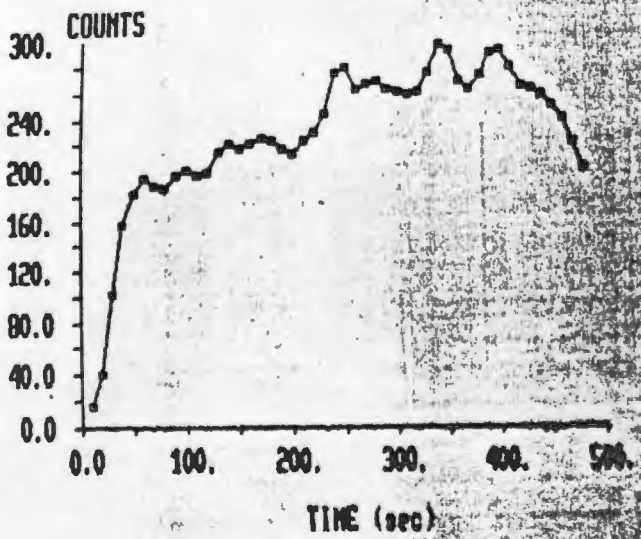
JOHNSTONE,R 86/3225 68313 691
PLACENTA



#49 SUMMED IMAGES:1-48

BASELINE 1 8/11/86 7:28

BASELINE 1



BASELINE 1 8/11/86 7:28

UTERO-PLACENTA BLOOD FLOW

BASELINE 1

100% = 210

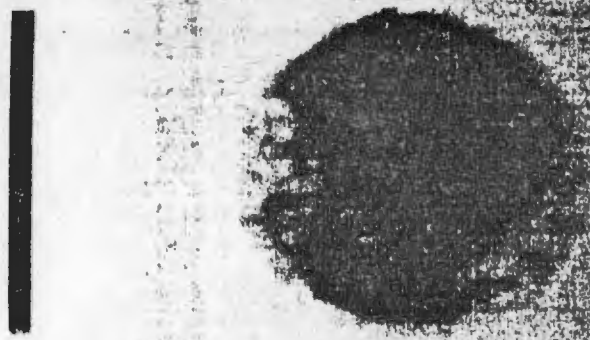
90% = 200

5% = 11

RISE TIME = 66 sec

UPBFI = 3.2

JOHNSTONE,R 86/3225 68313 631



#49 SUMMED IMAGES:1-48

BASELINE 2 8/11/86 8:14

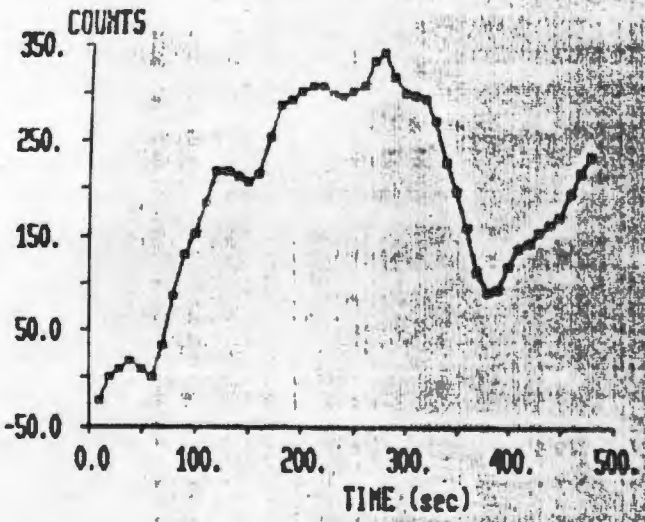
JOHNSTONE,R 86/3225 68313 631

PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 2 8/11/86 8:14

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 270 cts

90% = 257 cts

5% = 14 cts

RISE TIME = 86 sec

UPBFI = 3.1

JOHNSTONE,R 86/3225 68313 691

#49 SUMMED IMAGES:1-48

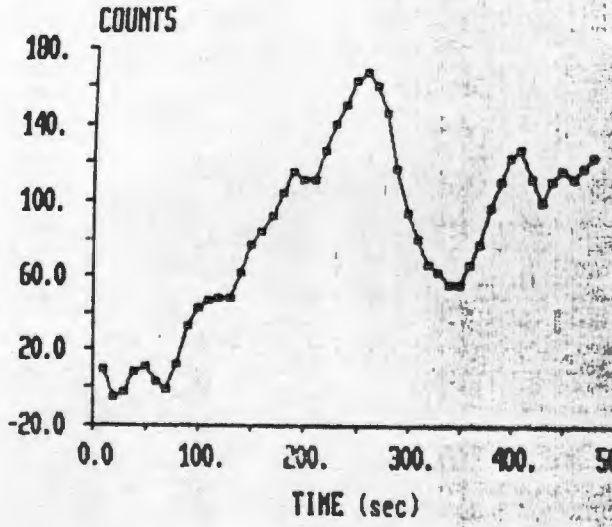
POST DRUG 8/11/86 8:38

JOHNSTONE,R 86/3225 68313 691
PLACENTA:ROI 2

#49 SUMMED IMAGES:1-48

POST [illegible] 8/11/86 8:39

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 135 cnts

90% = 128 cnts

5% = 7 cnts

RISE TIME = 140 sec

UPBFI = 1

PATIENT DATA

PATIENT NO.:	2
AGE: (YRS)	36
PARITY:	4
SMOKER:	No
GESTATIONAL AGE: (WKS)	35
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	10
PLATELET COUNT:	259
URIC ACID (m mol/L)	0.25
UREA (m mol/L)	2.9
CREATININE (m mol/L)	62

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	167
	Diastolic	114
	Mean arterial pressure	130
Mean post-treatment blood pressure:	Systolic	177
	Diastolic	119
	Mean arterial pressure	132
Mean pre-treatment pulse rate		111
Mean post-treatment pulse rate		110

2. BLOOD FLOW INDICES:

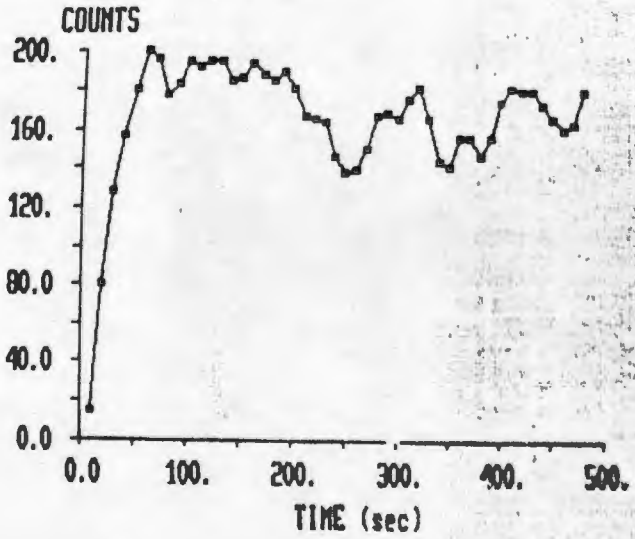
Pretreatment scan I	Maximum count rate	180
	Rise time	34
	Blood flow index	5.3
Pretreatment scan II	Maximum count rate	173
	Rise time	42
	Blood flow index	4.2
Post-treatment Scan	Maximum count rate	170
	Rise time	114
	Blood flow index	1.5

ABRAHAMS,S MM86/3110 67916 965

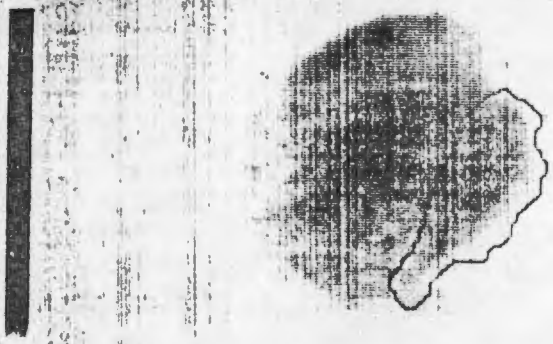
#49 SUMMED IMAGES:1-48

BASELINE 1 7/28/86 9:30

BASELINE 1



ABRAHAMS,S MM86/3110 67916 965
PLACENTA



#49 SUMMED IMAGES:1-48

BASELINE 1 7/28/86 9:30

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 180

50% = 171

5% = 9

RISE TIME = 34 sec

UPBFI = 5.3

ABRAHAMS,S MMB6/3110 67916 965

#49 SUMMED IMAGES:1-48

BASELINE 2 7/28/06 9:52

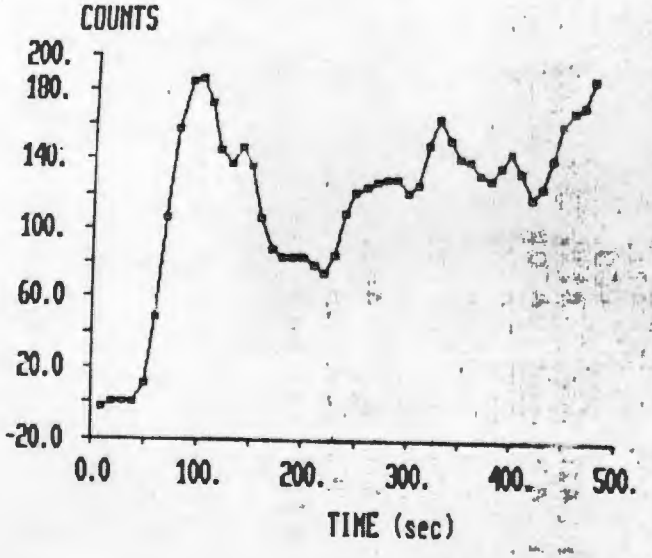
ABRAHAMS,S MMB6/3110 67916 965

PLACENTA 2

#49 SUMMED IMAGES:1-48

BASELINE 2 7/28/06 9:52

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 175 cnts

95% = 166 cnts

5% = 9 cnts

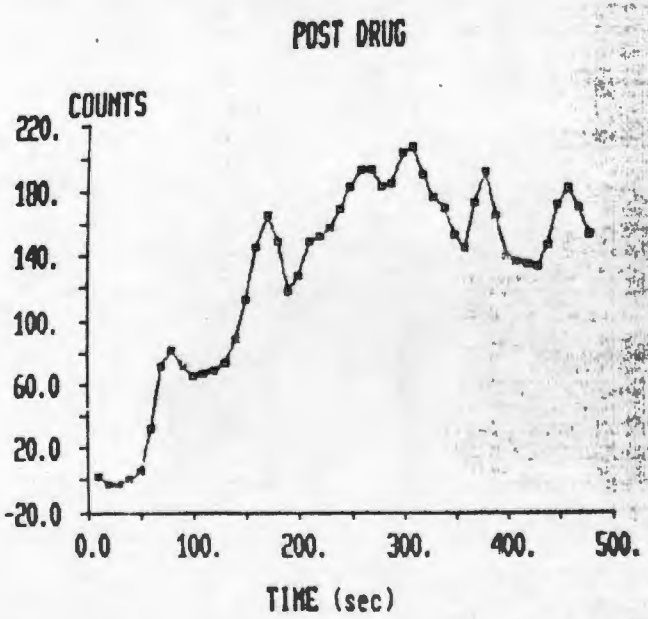
RISE TIME = 42 sec

UPBFI = 4.2

ABRAHAMS,S MM86/3110

#49 SUMMED IMAGES:1-48

POST DRUG 7/28/86 10:24



PLACENTA

#49 SUMMED IMAGES:1-48

POST DRUG 7/28/86 10:24

UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 170

90% = 162

5% = 9

RISE TIME = 114 sec

UPBFI = 1.5

PATIENT DATA

PATIENT NO.:	3
AGE: (YRS)	21
PARITY:	0
SMOKER:	No
GESTATIONAL AGE: (WKS)	32
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	10.6
PLATELET COUNT:	253
URIC ACID (m mol/L)	0.27
UREA (m mol/L)	2.5
CREATININE (m mol/L)	62

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	147
	Diastolic	97
	Mean arterial pressure	115
Mean post-treatment blood pressure:	Systolic	140
	Diastolic	93
	Mean arterial pressure	112
Mean pre-treatment pulse rate		88
Mean post-treatment pulse rate		75

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	165
	Rise time	70
	Blood flow index	2.4
Pretreatment scan II	Maximum count rate	175
	Rise time	82
	Blood flow index	2.1
Post-treatment Scan	Maximum count rate	175
	Rise time	79
	Blood flow index	2.2

LITTLE,R 06/2416 68411 321

SUMMED IMAGES 1-48

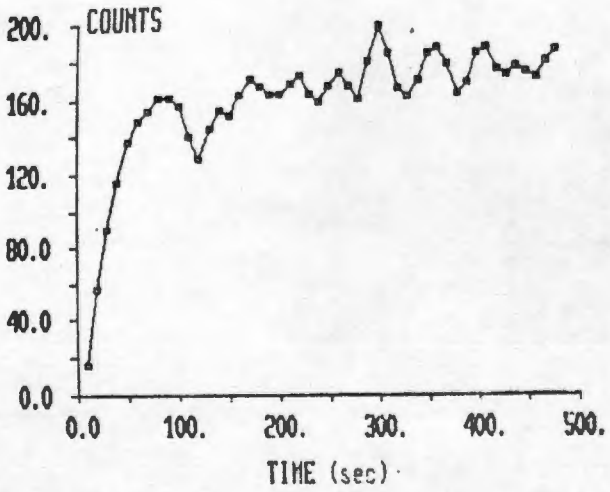
BASELINE 1 6/ 9/86 14:53

LITTLE,R 06/2416 68411 321
PLACENTA

SUMMED IMAGES 1-48

BASELINE 1 6/ 9/86 14:53

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 165 cts

95% = 157 cts

5% = 8 cts

RISE TIME = 70 sec

UPBFI = 2,36

LITTLE,R 86/2416 68411 321

SUMMED IMAGES 1-48

BASELINE 2 6/ 9/86 15:18

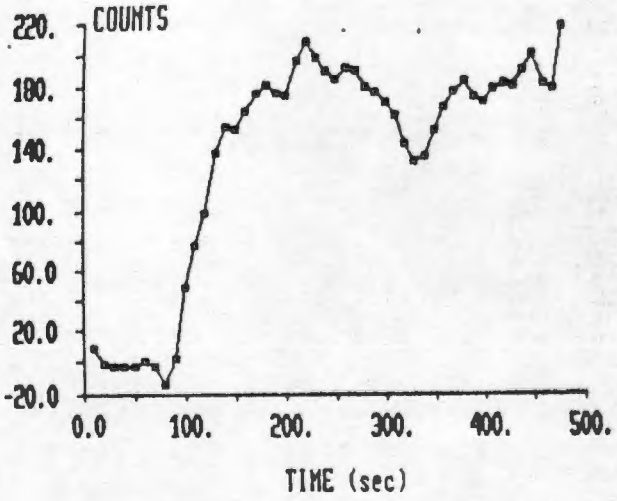
LITTLE,R 86/2416 68411 321

PLACENTA

SUMMED IMAGES 1-48

BASELINE 2 6/ 9/86 15:18

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 175 cts

95% = 166 cts

5% = 9 cts

RISE TIME = 82 sec

UPBFI = 2,13

LITTLE,R 06/2416 60411 321

SUMMED IMAGES 1-48

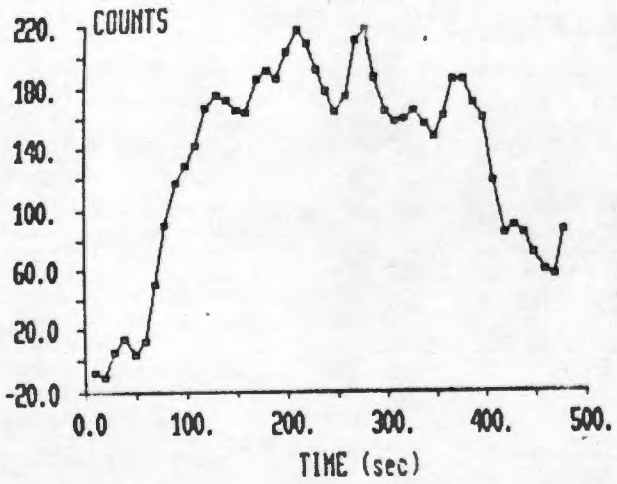
POST DRUG 6/ 9/86 15:57

PLACENTA

SUMMED IMAGES 1-48

POST DRUG 6/ 9/86 15:57

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 175 cts

95% = 166 cts

5% = 9 cts

RISE TIME = 79 sec

UPBFI = 2,22

PATIENT DATA

PATIENT NO.:	4
AGE: (YRS)	35
PARITY:	1
SMOKER:	Yes
GESTATIONAL AGE: (WKS)	35
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	1.2 g/ 24 hrs
HAEMOGLOBIN (g%)	11.6
PLATELET COUNT:	401
URIC ACID (m mol/L)	0.34
UREA (m mol/L)	2.5
CREATININE (m mol/L)	70

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	143
	Diastolic	89
	Mean arterial pressure	105
Mean post-treatment blood pressure:	Systolic	141
	Diastolic	93
	Mean arterial pressure	104
Mean pre-treatment pulse rate		83
Mean post-treatment pulse rate		80

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	160
	Rise time	78
	Blood flow index	2.1
Pretreatment scan II	Maximum count rate	140
	Rise time	48
	Blood flow index	2.9
Post-treatment Scan	Maximum count rate	210
	Rise time	114
	Blood flow index	1.8

ADONIS,S MM86/3601

#49 SUMMED IMAGES:1-48

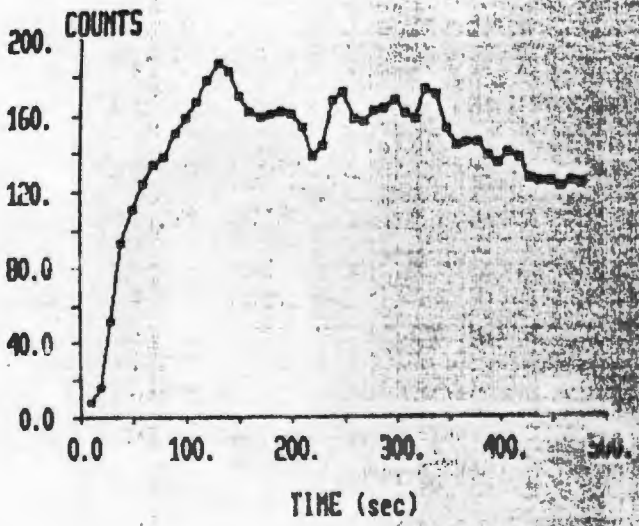
BASELINE 1 8/19/86 8:21

ADONIS,S MM86/3601
PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 1 8/19/86 8:21

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 160 cnts

90% = 152 cnts

5% = 8 cnts

RISE TIME = 2.05

ADONIS,S MM86/3601 68661 883

#49 SUMMED IMAGES:1-49

BASELINE 2 8/19/86 9:36

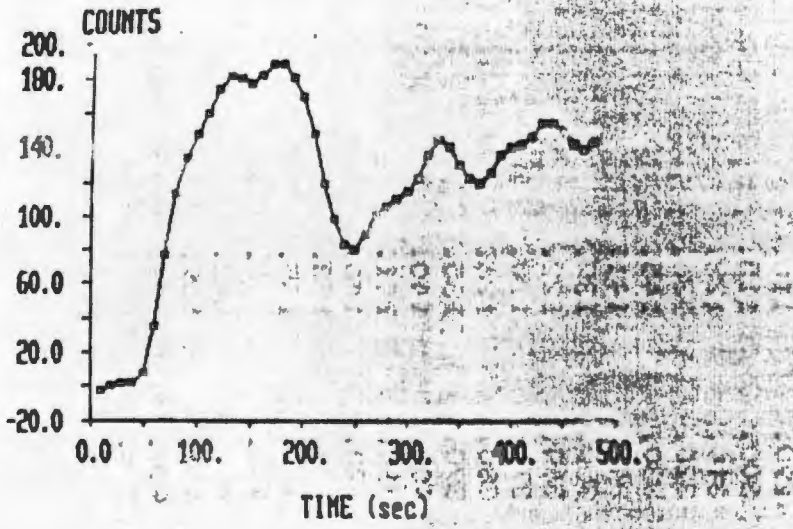
ADONIS,S MM86/3601 68661 883

PLACENTA

#49 SUMMED IMAGES:1-49

BASELINE 2 8/19/86 9:36

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 140 cnts

90% = 133 cnts

5% = 7 cnts

RISE TIME = 48 sec

UPBFI = 2.9

ADONIS,S MM86/3601 68661 883

#49 SUMMED IMAGES:1-48

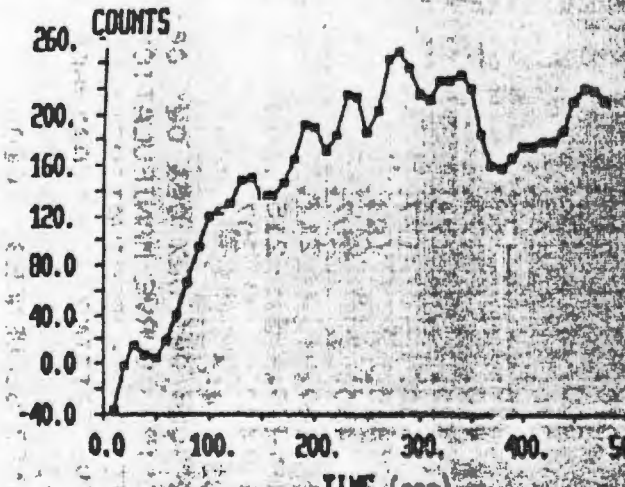
POST DRUG 8/19/86 10:07

ADONIS,S MM86/3601 68661 883
PLACENTA

#49 SUMMED IMAGES:1-48

POST DRUG 8/19/86 10:07

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 210 cnts
95% = 200 cnts
5% = 11 cnts
RISE TIME = 114 sec
UPBFI = 1.8

PATIENT DATA

PATIENT NO.:	5
AGE: (YRS)	25
PARITY:	3
SMOKER:	No
GESTATIONAL AGE: (WKS)	34
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	3+ (Cold test)
HAEMOGLOBIN (g%)	12.1
PLATELET COUNT:	237
URIC ACID (m mol/L)	0.44
UREA (m mol/L)	5.0
CREATININE (m mol/L)	79

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	168
	Diastolic	110
	Mean arterial pressure	127
Mean post-treatment blood pressure:	Systolic	169
	Diastolic	113
	Mean arterial pressure	130
Mean pre-treatment pulse rate		76
Mean post-treatment pulse rate		80

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	175
	Rise time	70
	Blood flow index	2.5
Pretreatment scan II	Maximum count rate	170
	Rise time	83
	Blood flow index	2
Post-treatment Scan	Maximum count rate	210
	Rise time	79
	Blood flow index	2.7

CENTRE,M 86/1803, 54083 8033

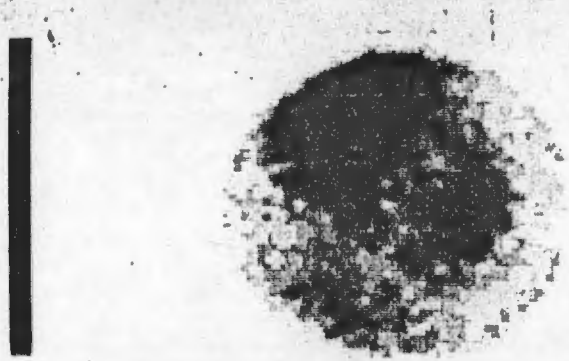


IMAGE #1

U.P. BLOOD FLOW BASE 1 4/29/86 15:17

CENTRE,M 86/1803 54083 8033
PLACENTA 1

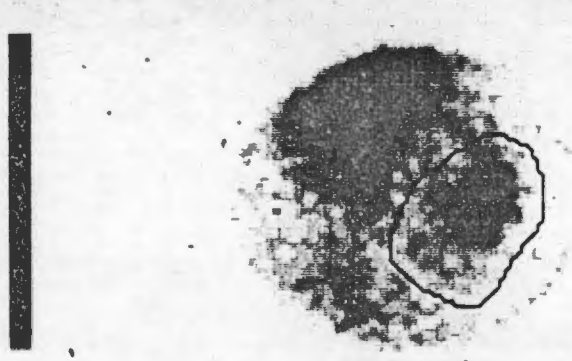
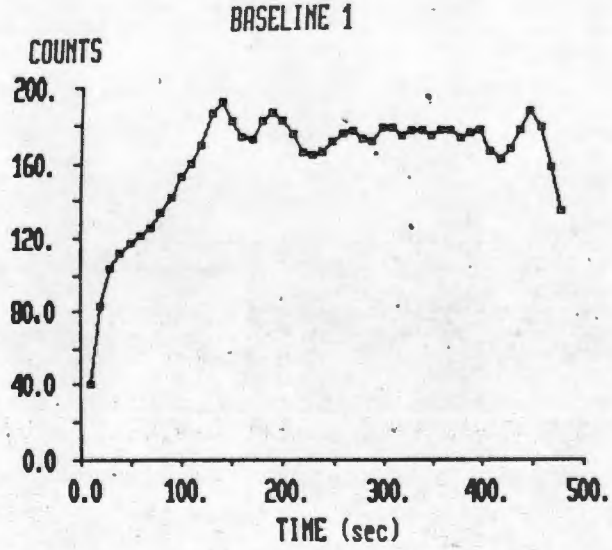


IMAGE #1

U.P. BLOOD FLOW BASE 1 4/29/86 15:17



UTERO-PLACENTAL BLOOD FLOW

RISE TIME: [illegible] sec 70

100% : 175 cts

5% : 8,8 cts

95% : 166,3 cts

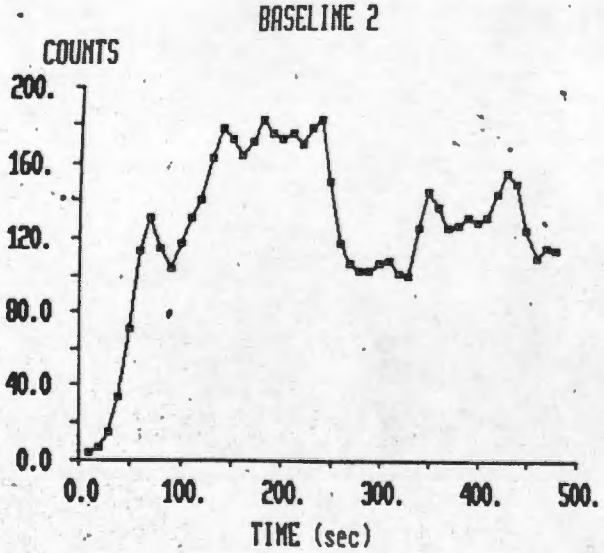
UPBFI : [illegible] 2·5

IMAGE #1

U.P. BLOOD FLOW BASE 2 4/29/86 15:58

IMAGE #1

U.P. BLOOD FLOW BASE 2 4/29/86 15:58



UTERO-PLACENTAL BLOOD FLOW

RISE TIME: [redacted] sec 83

100% : 170 cts

5% : 8,5 cts

95% : 161,5 cts

UPBFI : [redacted] 2·0

CENTRE,N 86/1803 54083 0033

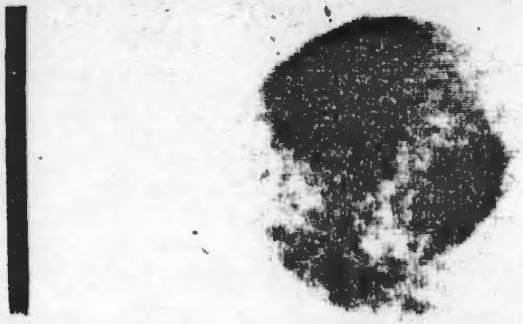
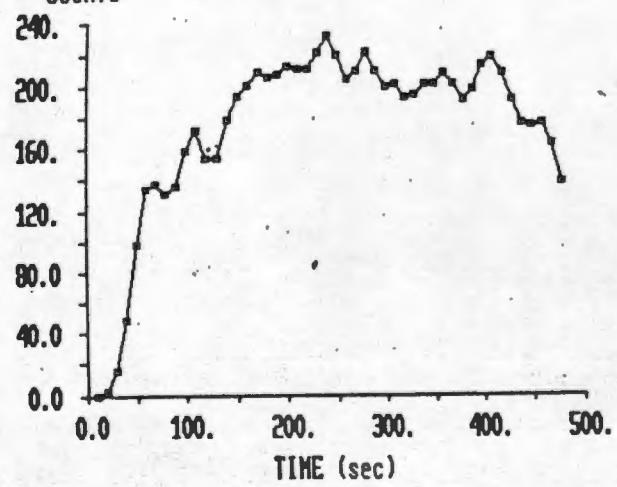


IMAGE #1

U.P. BLOOD FLOW DRUG 4/29/86 16:41

POST DRUG



PLACENTA 1

IMAGE #1

U.P. BLOOD FLOW DRUG 4/29/86 16:41

UTERO-PLACENTAL BLOOD FLOW

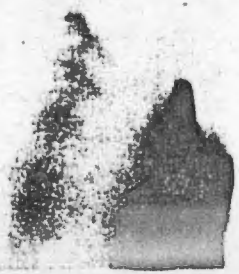
RISE TIME: [illegible] sec 79

100% : 210 cts

5% : 10,5 cts

95% : 199,5 cts

UPBFI : [illegible] 2·7



PATIENT DATA

PATIENT NO.:	6
AGE: (YRS)	20
PARITY:	0
SMOKER:	Yes
GESTATIONAL AGE: (WKS)	34
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	0.74 g/24 hr
HAEMOGLOBIN (g%)	10.5
PLATELET COUNT:	164
URIC ACID (m mol/L)	0.4
UREA (m mol/L)	3.6
CREATININE (m mol/L)	79

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	154
	Diastolic	111
	Mean arterial pressure	125
Mean post-treatment blood pressure:	Systolic	150
	Diastolic	110
	Mean arterial pressure	125
Mean pre-treatment pulse rate		80
Mean post-treatment pulse rate		86

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	225
	Rise time	97
	Blood flow index	2.3
Pretreatment scan II	Maximum count rate	-
	Rise time	-
	Blood flow index	-
Post-treatment Scan	Maximum count rate	350
	Rise time	112
	Blood flow index	3.1

THEBUS,P 86/2107 68191 865

SUMMED IMAGES 1-48

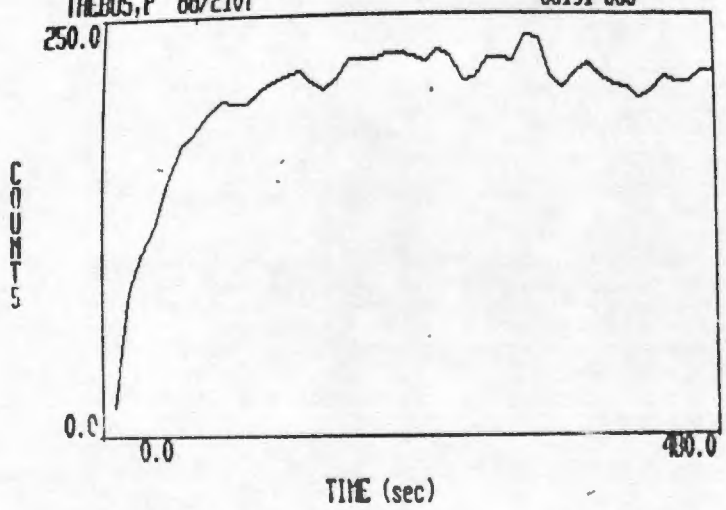
BASELINE 1 5/21/86 9:42

THEBUS,P 86/2107
PLACENTA:BASE 1

SUMMED IMAGES 1-48

BASELINE 1 5/21/86 9:42

THEBUS,P 86/2107 68191 865



CBV:BASELINE 1 6/ 6/86 11:51

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 225 cts

95% = 214 cts

5% = 11 cts

RISE TIME = 97 sec

UPDFI = 2.32

THEBUS,P 06/2107 68191 865

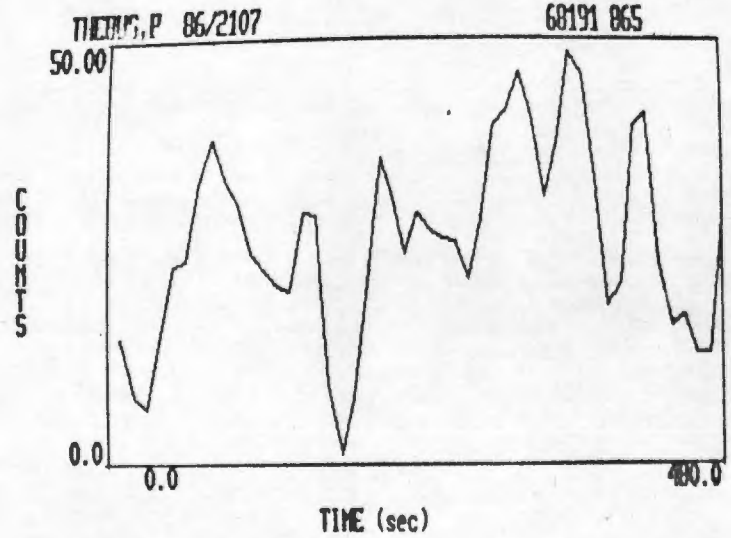
SUMMED IMAGES 1-48

BASELINE 2 5/21/86 10:13

THEBUS,P 06/2107 68191 865
PLACENTA

SUMMED IMAGES 1-48

BASELINE 2 5/21/86 10:13



CRV:BASELINE 2 6/ 6/86 14:41

VERY POOR CURVE.

? CORRECT DOSE

? INTERSTITIAL INJECTION

CANNOT CALCULATE ANYTHING

THEBUS,P 86/2107 68191 865

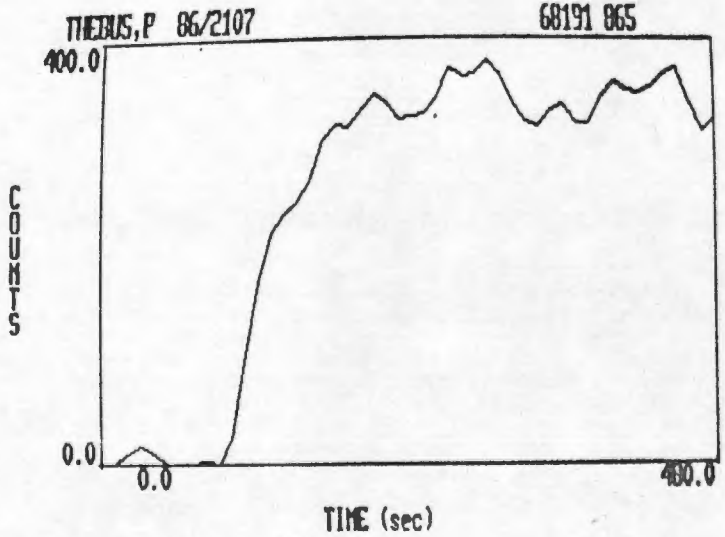
SUMMED IMAGES 1-48

POST DRUG 5/21/86 10:40

THEBUS,P 86/2107
PLACENTA

SUMMED IMAGES 1-48

POST DRUG 5/21/86 10:40



CRV:POST DRUG 6/ 6/86 12:36

UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 350 cts

95% = 333 cts

5 % = 18 cts

RISE TIME = 112 sec

UPBFI = 3,13

PATIENT DATA

PATIENT NO.:	7
AGE: (YRS)	17
PARITY:	0
SMOKER:	No
GESTATIONAL AGE: (WKS)	36
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	12
PLATELET COUNT:	211
URIC ACID (m mol/L)	0.32
UREA (m mol/L)	2.1
CREATININE (m mol/L)	53

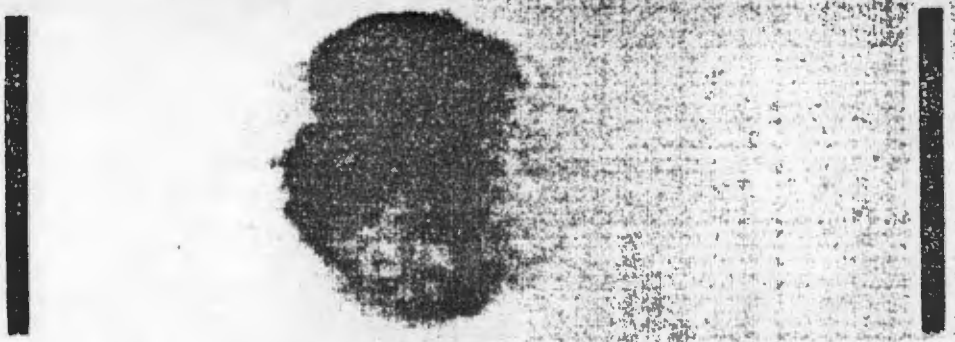
1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	147
	Diastolic	94
	Mean arterial pressure	112
Mean post-treatment blood pressure:	Systolic	152
	Diastolic	98
	Mean arterial pressure	117
Mean pre-treatment pulse rate		98
Mean post-treatment pulse rate		90

2. BLOOD FLOW INDICES:

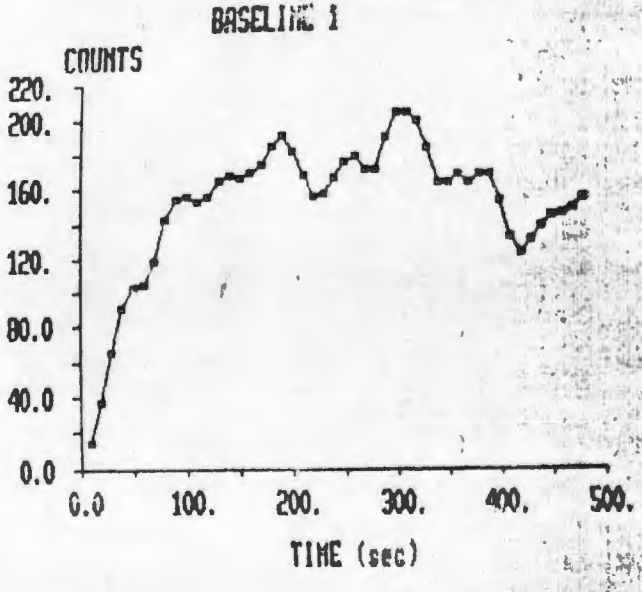
Pretreatment scan I	Maximum count rate	190
	Rise time	122
	Blood flow index	1.7
Pretreatment scan II	Maximum count rate	155
	Rise time	139
	Blood flow index	1.1
Post-treatment Scan	Maximum count rate	205
	Rise time	73
	Blood flow index	2.8

NILSON,L 86/2876 68345 701



#49 SUMMED IMAGES 1-48

BASELINE 1 7/10/86 9:39



NILSON,L 86/2876
PLACENTA

#49 SUMMED IMAGES 1-48

BASELINE 1 7/10/86 9:39

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 190 cts
95% = 181 cts
5% = 10 cts
RISE TIME = 122 sec
UPBFI = 1,7

WILSON,L 86/2876 68345 701

#49 SUMMED IMAGES 1-48

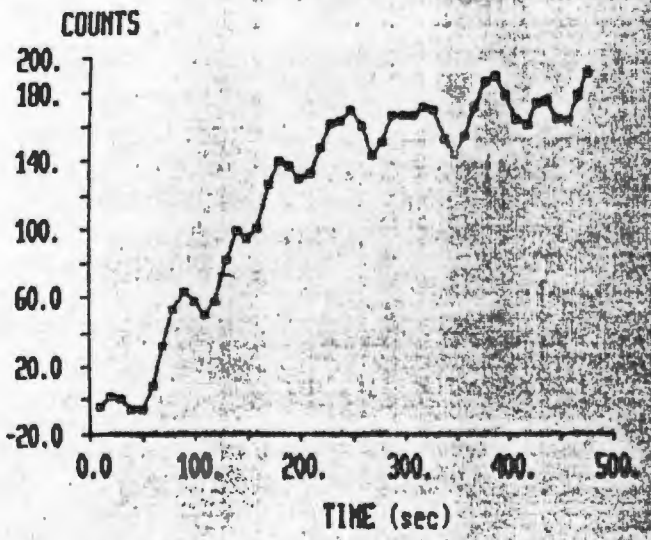
BASELINE 2 7/10/86 10:13

WILSON,L 86/2876 68345 701
PLACENTA ROI:2

#49 SUMMED IMAGES 1-48

BASELINE 2 7/10/86 10:13

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 155 cts
95% = 147 cts
5% = 8 cts
RISE TIME = 139 sec
UPBFI = 1.1

WILSON,L 86/2876

#49 SUMMED IMAGES 1-48

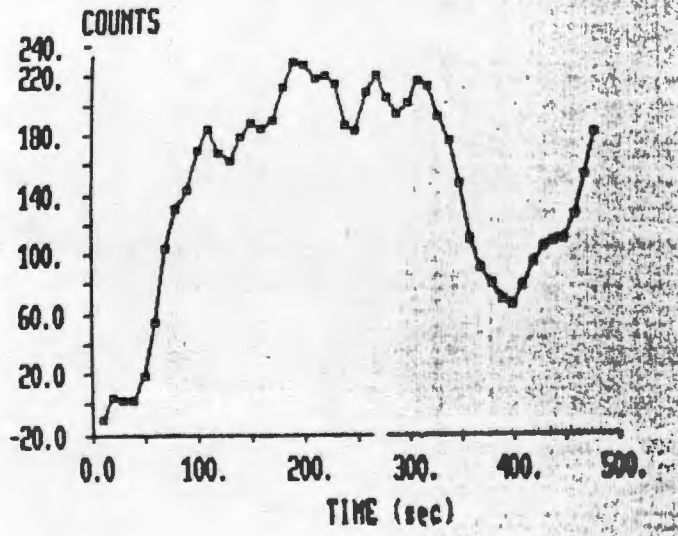
POST DRUG 7/10/86 11:05

WILSON,L
PLACENTA

#49 SUMMED IMAGES 1-48

POST DRUG 7/10/86 11:05

POST DRUG



UTERO-PLACENTA BLOOD FLOW

POST DRUG

100% = 205

90% = 195

5% = 10

RISE TIME = 73 sec

UPBFI = 2.8

PATIENT DATA

PATIENT NO.:	8
AGE: (YRS)	42
PARITY:	2
SMOKER:	No
GESTATIONAL AGE: (WKS)	32
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	11.9
PLATELET COUNT:	234
URIC ACID (m mol/L)	0.19
UREA (m mol/L)	1.8
CREATININE (m mol/L)	62

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	138
	Diastolic	98
	Mean arterial pressure	109
Mean post-treatment blood pressure:	Systolic	140
	Diastolic	102
	Mean arterial pressure	114
Mean pre-treatment pulse rate		85
Mean post-treatment pulse rate		88

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	160
	Rise time	82
	Blood flow index	2
Pretreatment scan II	Maximum count rate	185
	Rise time	75
	Blood flow index	2.5
Post-treatment Scan	Maximum count rate	205
	Rise time	69
	Blood flow index	3

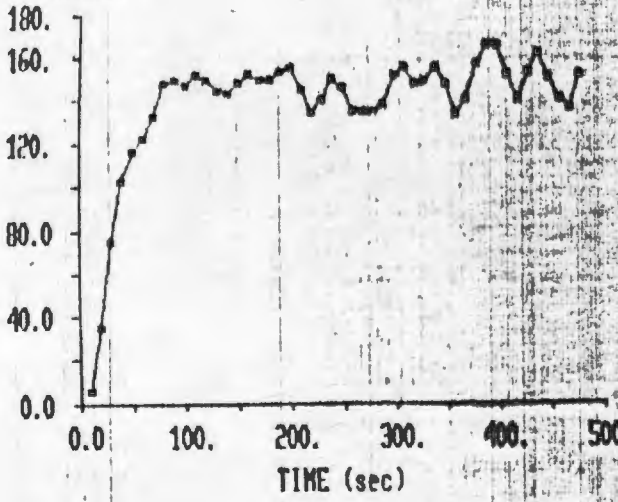
MARINUS,B MM86/2417 664766 629

#49 SUMMED IMAGES:1-48

BASELINE 1 6/10/86 8:34

BASELINE 1

COUNTS



MARINUS,B MM86/2417 664766 629

PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 1 6/10/86 8:34

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 160 cnts

95% = 152 cnts

5% = 8 cnts

RISE TIME = 82 sec

UPBFI = 2.0

MARINUS,B MM86/2417

IMAGE #1

BASELINE 2

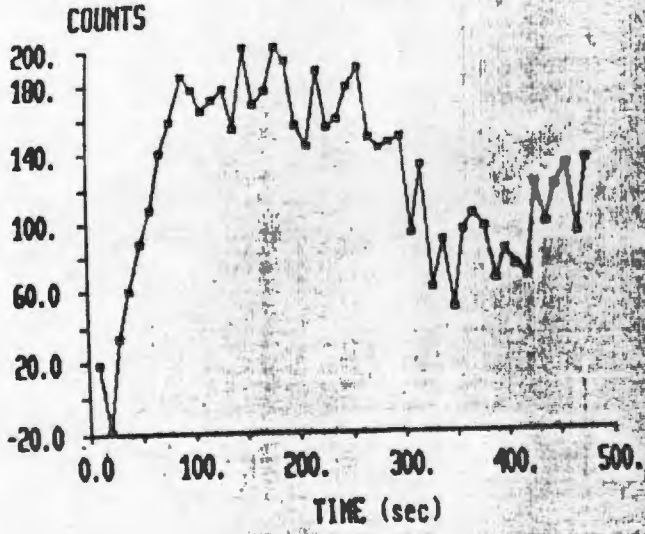
6/10/86 9:03

IMAGE #1

BASELINE 2

6/10/86 9:03

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 185 cnts

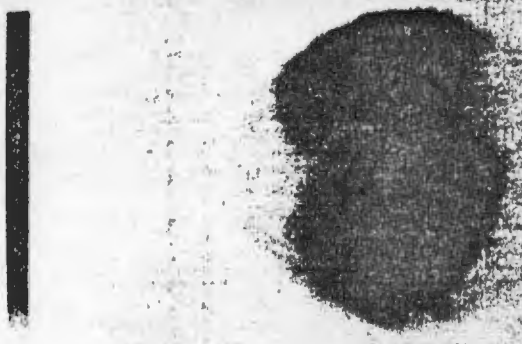
95% = 176 cnts

5% = 9 cnts

RISE TIME = 75 sec

UPBFI = 2.5

MARINUS,B · MM86/2417



#49 SUMMED IMAGES:1-49

POST DRUG

6/10/86 9:30

MARINUS,B MM86/2417

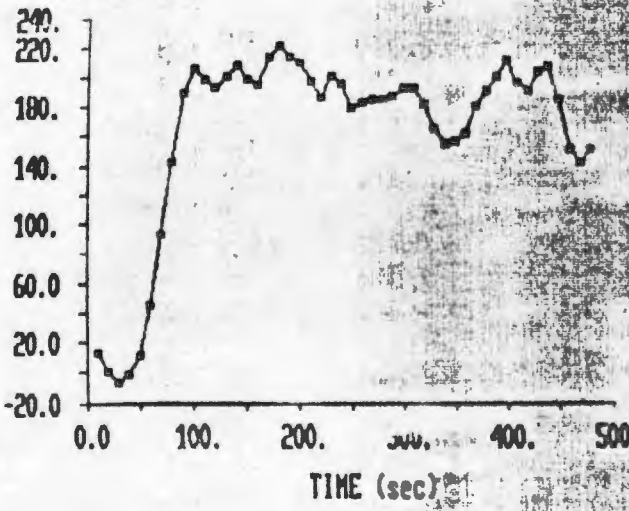
PLACENTA

#49 SUMMED IMAGES:1-49

POST DRUG

6/10/86 9:30

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 205 cnts

95% = 195 cnts

5% = 10 cnts

RISE TIME = 69 sec

UPBFI = 2.97

PATIENT DATA

PATIENT NO.:	9
AGE: (YRS)	30
PARITY:	2
SMOKER:	No
GESTATIONAL AGE: (WKS)	38
PLACEBO/MEDICINE:	Placebo
PROTEINURIA:	No
HAEMOGLOBIN (g%)	11.7
PLATELET COUNT:	194
URIC ACID (m mol/L)	0.34
UREA (m mol/L)	1.8
CREATININE (m mol/L)	53

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	128
	Diastolic	92
	Mean arterial pressure	103
Mean post-treatment blood pressure:	Systolic	128
	Diastolic	96
	Mean arterial pressure	104
Mean pre-treatment pulse rate		80
Mean post-treatment pulse rate		73

2. BLOOD FLOW INDICES:

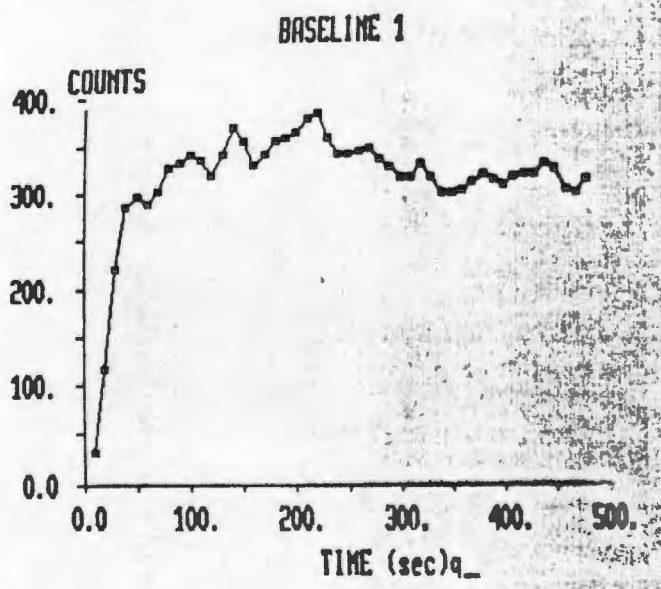
Pretreatment scan I	Maximum count rate	340
	Rise time	49
	Blood flow index	6.9
Pretreatment scan II	Maximum count rate	300
	Rise time	50
	Blood flow index	6
Post-treatment Scan	Maximum count rate	410
	Rise time	50
	Blood flow index	8.1

#49 SUMED IMAGES:1-48

BASELINE 1 7/31/86 16:16

#49 SUMED IMAGES:1-48

BASELINE 1 7/31/86 16:16



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 340 cnts

90% = 323 cnts

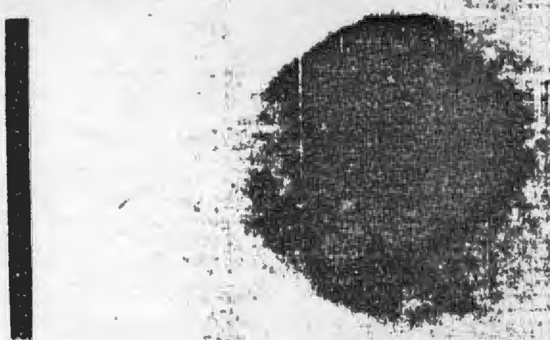
5% = 17 cnts

RISE TIME = 49 sec

UPBFI = 6.9

WARU,S MM86/3224

PLACENTA



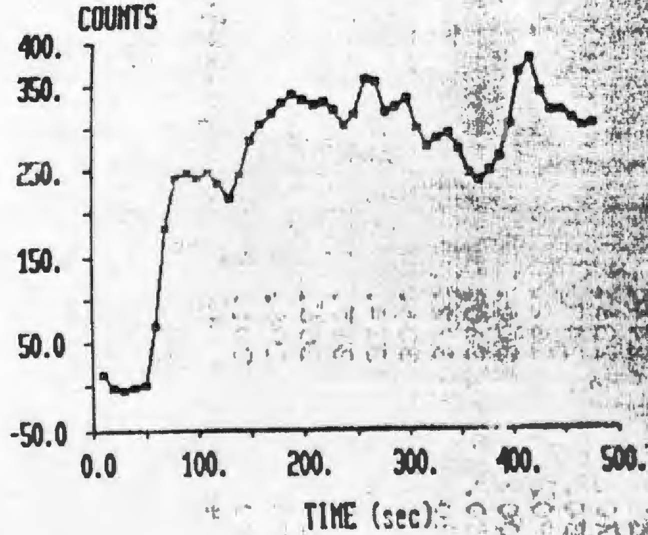
#49 SUMMED IMAGES:1-48

BASELINE 2 7/31/86 16:45

#49 SUMMED IMAGES:1-48

BASELINE 2 7/31/86 16:45

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 300 cnts

90% = 285 cnts

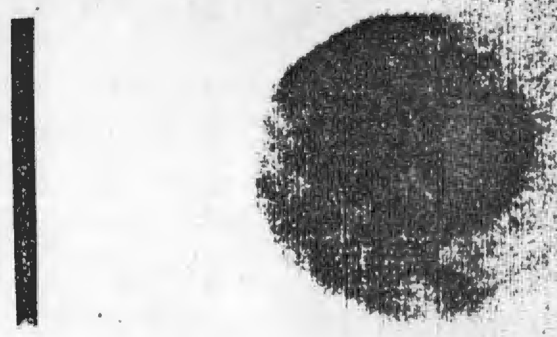
5% = 15 cnts

RISE TIME = 50 sec

U.P.B.F.I. = 6

WAGU,S MM86/3224 61624 003

PLACENTA



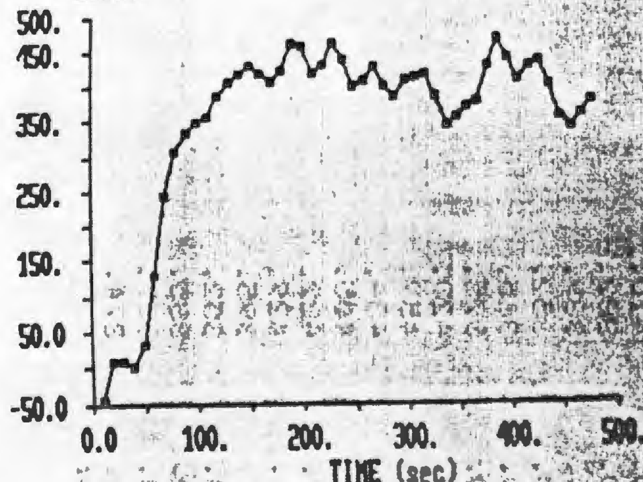
#49 SUMMED IMAGES:1-48

POST DRUG 7/31/86 17:09

#49 SUMMED IMAGES:1-48

POST DRUG 7/31/86 17:03

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 410 cnts

95% = 390 cnts

5% = 21 cnts

RISE TIME = 50 sec

UPBFI = 8.2

PATIENTS TREATED WITH NIFEDIPINE

PATIENT DATA

PATIENT NO.:	1
AGE: (YRS)	34
PARITY:	3
SMOKER:	No
GESTATIONAL AGE: (WKS)	37
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	No
HAEMOGLOBIN (g%)	11.3
PLATELET COUNT:	335
URIC ACID (m mol/L)	0.28
UREA (m mol/L)	1.8
CREATININE (m mol/L)	53

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	151
	Diastolic	96
	Mean arterial pressure	114
Mean post-treatment blood pressure:	Systolic	145
	Diastolic	89
	Mean arterial pressure	105
Mean pre-treatment pulse rate		84
Mean post-treatment pulse rate		81

2. BLOOD FLOW INDICES:

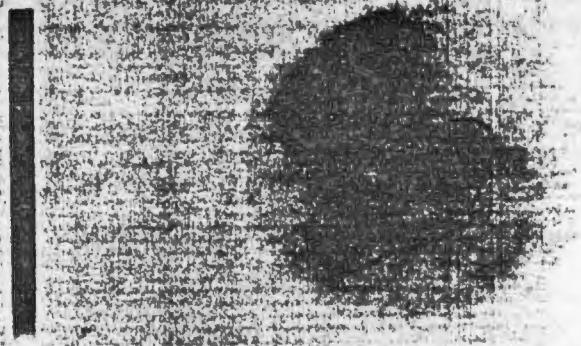
Pretreatment scan I	Maximum count rate	300
	Rise time	47
	Blood flow index	6.4
Pretreatment scan II	Maximum count rate	320
	Rise time	47
	Blood flow index	6.8
Post-treatment Scan	Maximum count rate	300
	Rise time	64
	Blood flow index	4.7

DAYIMANI,A 06/2752 54206 180

SUMMED IMAGES 1-48

BASELINE 1 7/ 2/86 8:20

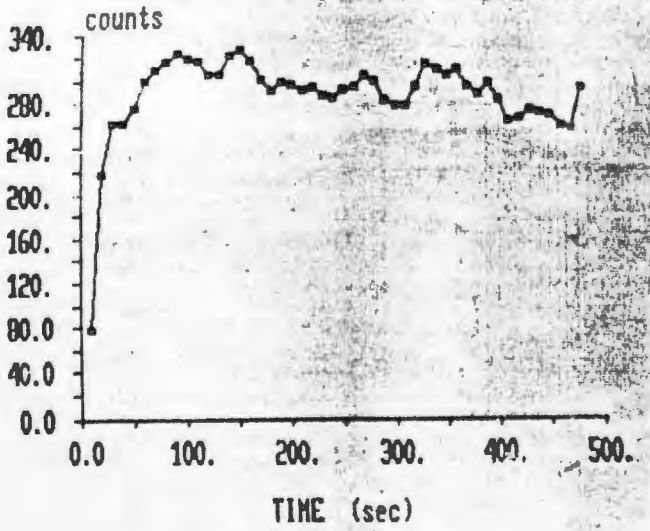
DAYIMANI,A 06/2752
PLACENTA



SUMMED IMAGES 1-48

BASELINE 1 7/ 2/86 8:20

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 300 cts

95% = 285 cts

5% = 15 cts

RISE TIME = 47 sec

UPBFI = 6,38

DAYIMANI,A 86/2752 54206 180

SUMMED IMAGES 1-48

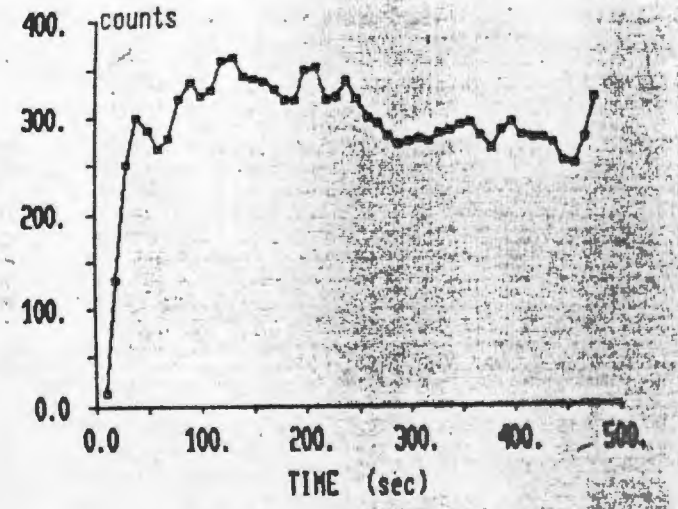
BASELINE 2 7/ 2/86 9:09

DAYIMANI,A 86/2752
PLACENTA

SUMMED IMAGES 1-48

BASELINE 2 7/ 2/86 9:09

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 320 cts

95% = 304 cts

5% = 16 cts

RISE TIME = 47 sec

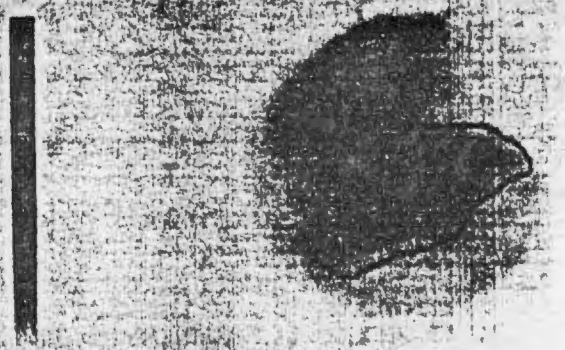
UPDFI = 6.81

DAYIMANI,A 06/2752

SUMMED IMAGES 1-48

POST DRUG 7/ 2/86 9:33

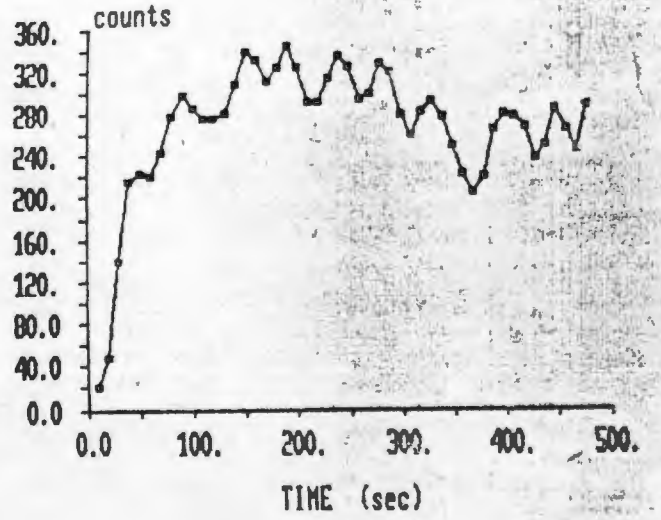
PLACENTA



SUMMED IMAGES 1-48

POST DRUG 7/ 2/86 9:33

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 300 cts

95% = 285 cts

5% = 15 cts

RISE TIME = 64 sec

UPBFI = 4,69

PATIENT DATA

PATIENT NO.:	2
AGE: (YRS)	25
PARITY:	2
SMOKER:	Yes
GESTATIONAL AGE: (WKS)	34
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	>3g/24 hrs
HAEMOGLOBIN (g%)	12.6
PLATELET COUNT:	321
URIC ACID (m mol/L)	0.35
UREA (m mol/L)	3.2
CREATININE (m mol/L)	62

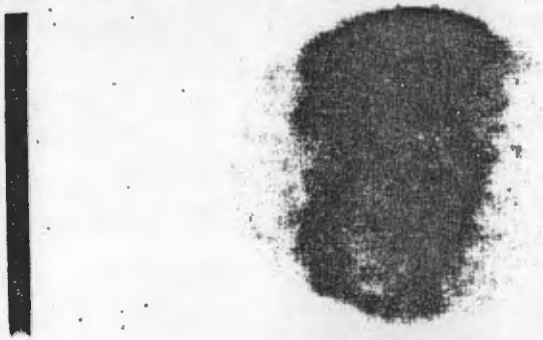
1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	141
	Diastolic	97
	Mean arterial pressure	116
Mean post-treatment blood pressure:	Systolic	119
	Diastolic	83
	Mean arterial pressure	105
Mean pre-treatment pulse rate		90
Mean post-treatment pulse rate		96

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	120
	Rise time	71
	Blood flow index	1.7
Pretreatment scan II	Maximum count rate	155
	Rise time	140
	Blood flow index	1.1
Post-treatment Scan	Maximum count rate	165
	Rise time	121
	Blood flow index	1.4

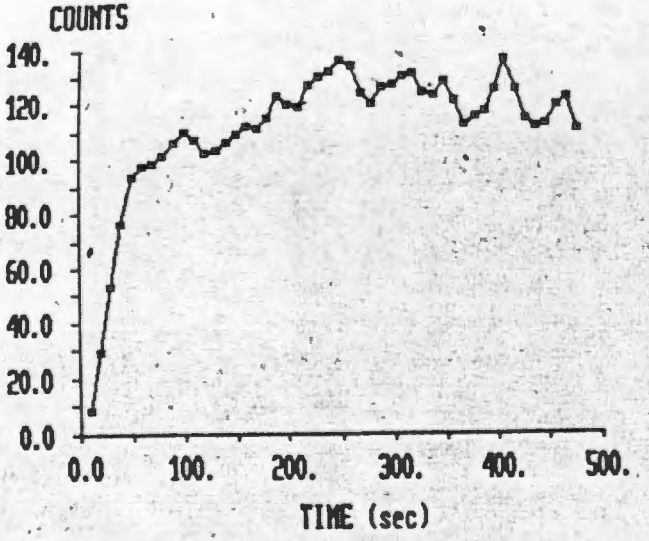
DARIES,R 86/3684 68751 148



#49 SUMMED IMAGES:1-48

BASELINE 1 8/ 2/86 7:39

BASELINE 1



DARIES,R 86/3684 68751 148
PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 1 8/ 2/86 7:39

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 120 cnts

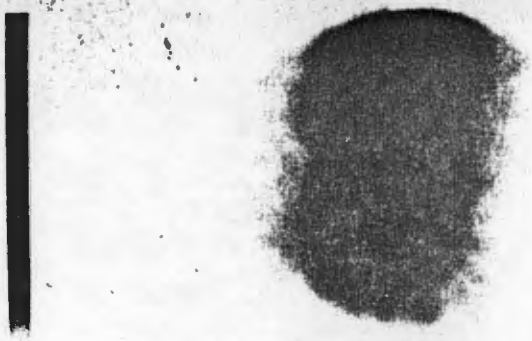
95% = 114 cnts

5% = 6 cnts

RISE TIME = 71 sec

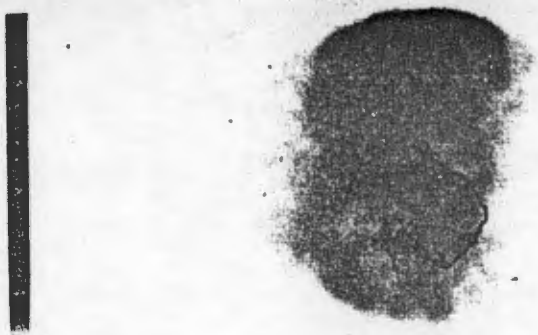
UPBFI = 1.7

PLACENTA



#49 SUMMED IMAGES:1-48

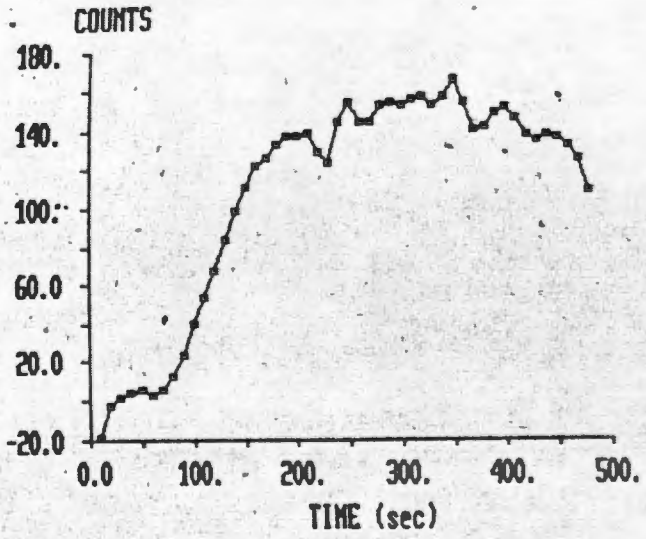
BASELINE 2 8/ 2/86 8:10



#49 SUMMED IMAGES:1-48

BASELINE 2 8/ 2/86 8:10

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 155 cnts

95% = 147 cnts

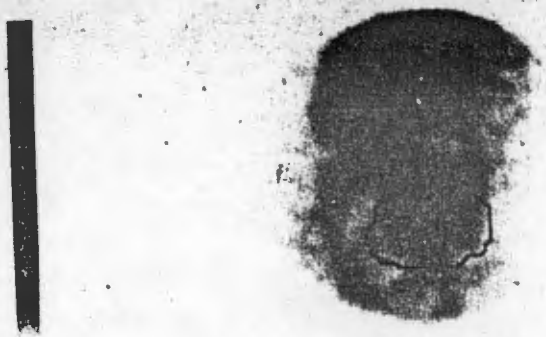
5% = 8 cnts

RISE TIME = 140 sec

UPBFI = 1.1

#49 SUMMED IMAGES:1-48

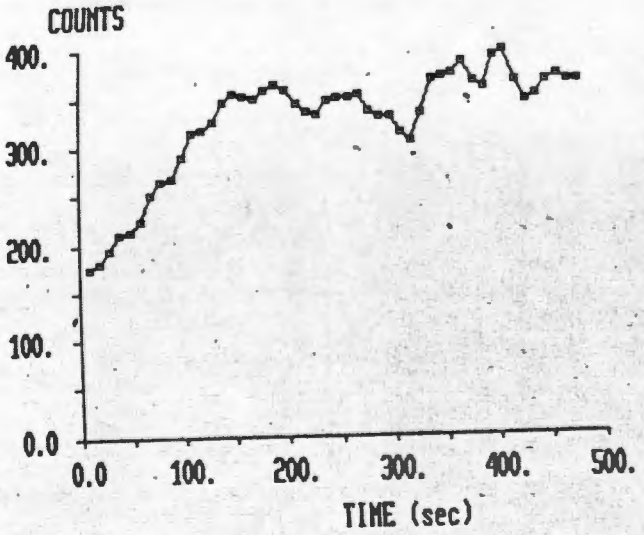
POST DRUG 8/ 2/86 8:46



#49 SUMMED IMAGES:1-48

POST DRUG 8/ 2/86 8:46

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 165 cnts

95% = 157 cnts

5% = 8 cnts

RISE TIME = 121 sec

UPBFI = 1.4

PATIENT DATA

PATIENT NO.:	3
AGE: (YRS)	22
PARITY:	0
SMOKER:	No
GESTATIONAL AGE: (WKS)	36
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	2+ (Cold test)
HAEMOGLOBIN (g%)	99
PLATELET COUNT:	296
URIC ACID (m mol/L)	0.45
UREA (m mol/L)	5.4
CREATININE (m mol/L)	70

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	155
	Diastolic	100
	Mean arterial pressure	115
Mean post-treatment blood pressure:	Systolic	153
	Diastolic	102
	Mean arterial pressure	112
Mean pre-treatment pulse rate		105
Mean post-treatment pulse rate		119

2. BLOOD FLOW INDICES:

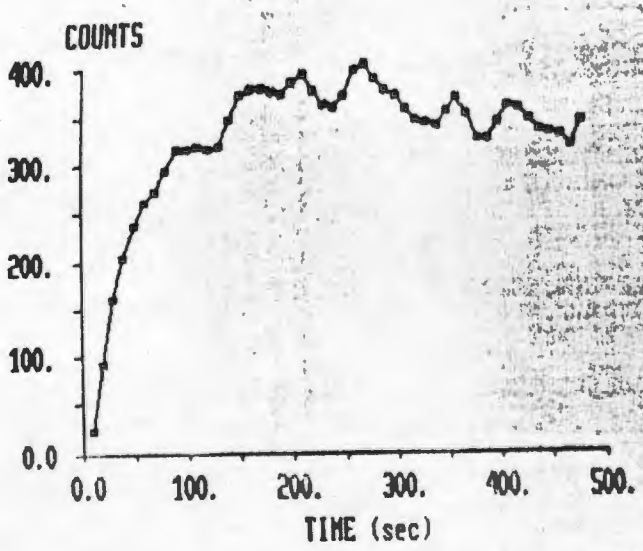
Pretreatment scan I	Maximum count rate	380
	Rise time	115
	Blood flow index	3.3
Pretreatment scan II	Maximum count rate	340
	Rise time	68
	Blood flow index	5
Post-treatment Scan	Maximum count rate	470
	Rise time	103
	Blood flow index	4.6

HOPE,L 886/3356 68683 804

#49 SUMMED IMAGES:1-48

BASELINE 1 8/11/86 16:22

BASELINE 1



HOPE,L PLACENTA 886/3356

#49 SUMMED IMAGES:1-48

BASELINE 1 8/11/86 16:22

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 380 cnts

90% = 361 cnts

RISE TIME = 115 sec

UPBFI = 3.3

HOPE,L 886/3356 60683 804

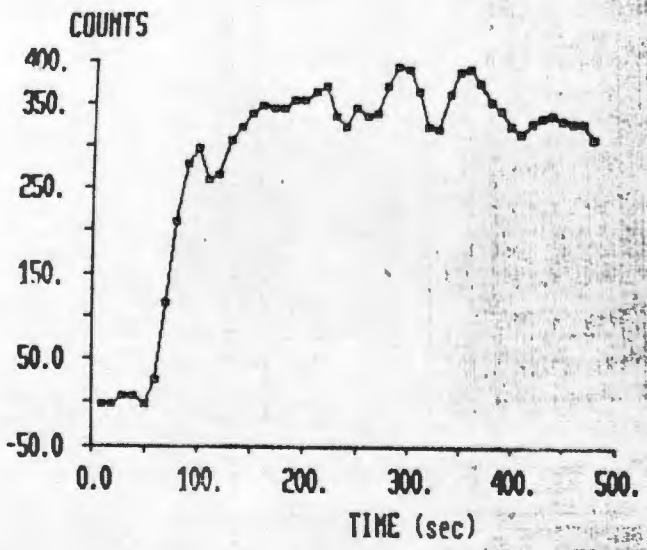
IMAGE #1

HOPE,L 886/3356 60683 804
PLACENTA

IMAGE #1

BASELINE 2 8/11/06 17:14

BASELINE 2



BASELINE 2 8/11/06 17:14

UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

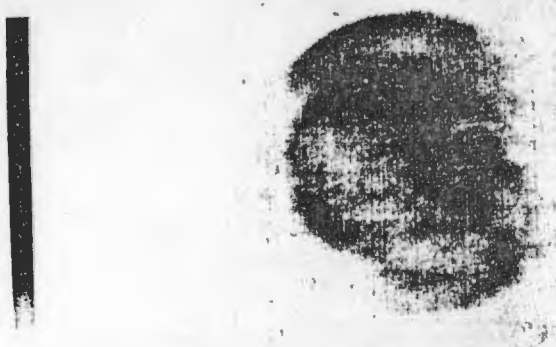
100% = 340 cnts

95% = 323 cnts

RISE TIME = 68 sec

UPBFI = 5

HOPE,L 886/3356

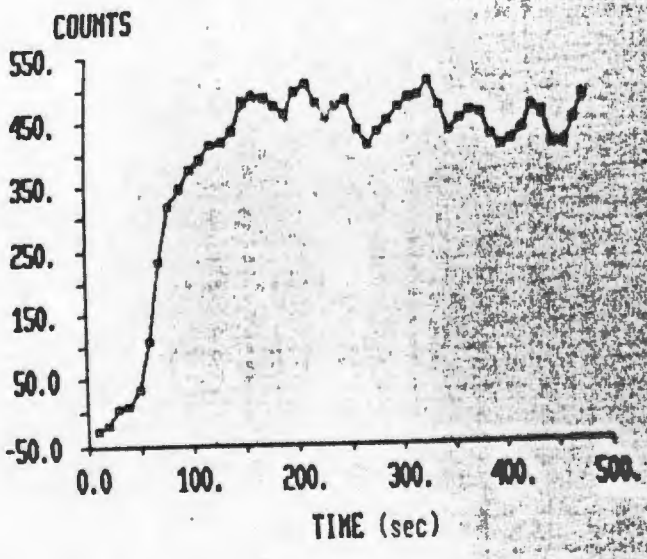


#49 SUMMED IMAGES:1-48

POST DRUG

8/11/06 17:43

POST DRUG



PLACENTA

#49 SUMMED IMAGES:1-48

POST DRUG

8/11/06 17:43

UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 470 cnts

95% = 447 cnts

5% = 24 cnts

RISE TIME = 103 sec

UPBFI = 4.6

PATIENT DATA

PATIENT NO.:	4
AGE: (YRS)	23
PARITY:	0
SMOKER:	No
GESTATIONAL AGE: (WKS)	37
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	No
HAEMOGLOBIN (g%)	8.7
PLATELET COUNT:	199
URIC ACID (m mol/L)	0.26
UREA (m mol/L)	3.9
CREATININE (m mol/L)	62

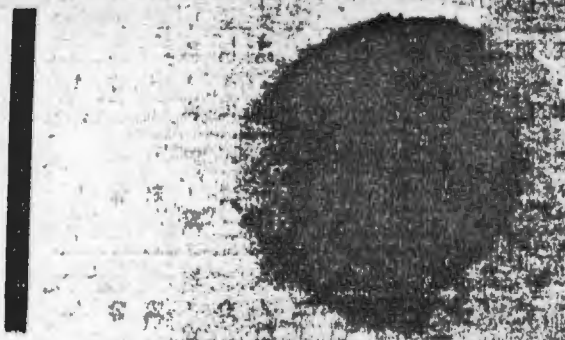
1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	141
	Diastolic	98
	Mean arterial pressure	113
Mean post-treatment blood pressure:	Systolic	140
	Diastolic	94
	Mean arterial pressure	108
Mean pre-treatment pulse rate		87
Mean post-treatment pulse rate		105

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	290
	Rise time	51
	Blood flow index	5.7
Pretreatment scan II	Maximum count rate	330
	Rise time	60
	Blood flow index	5.5
Post-treatment Scan	Maximum count rate	340
	Rise time	86
	Blood flow index	4

PECK,A 86/3044 68364 652

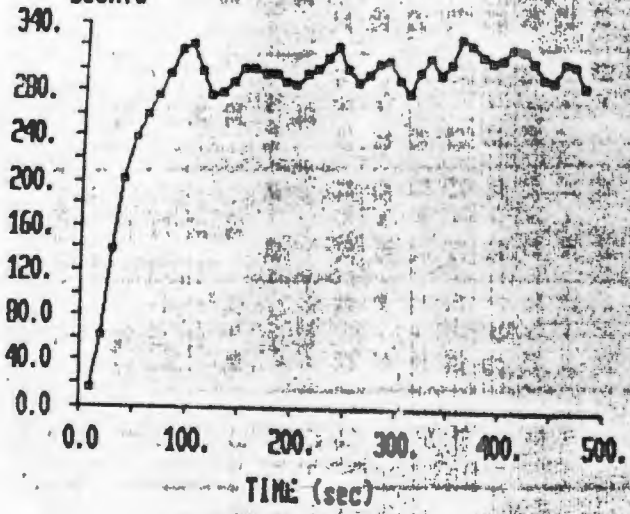


48 SUMMED IMAGES:1-48

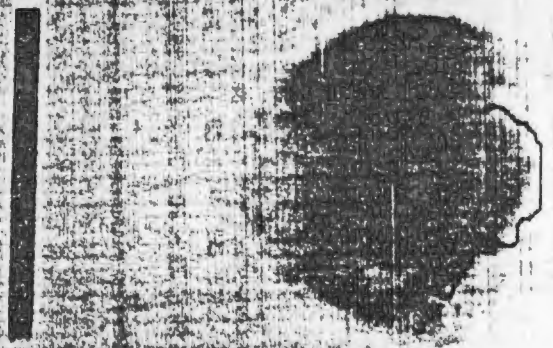
BASELINE 1 7/23/86 8:50

BASELINE 1

COUNTS



PECK,A 86/3044 68364 652
PLACENTA



48 SUMMED IMAGES:1-48

BASELINE 1 7/23/86 8:50

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 290 cnts

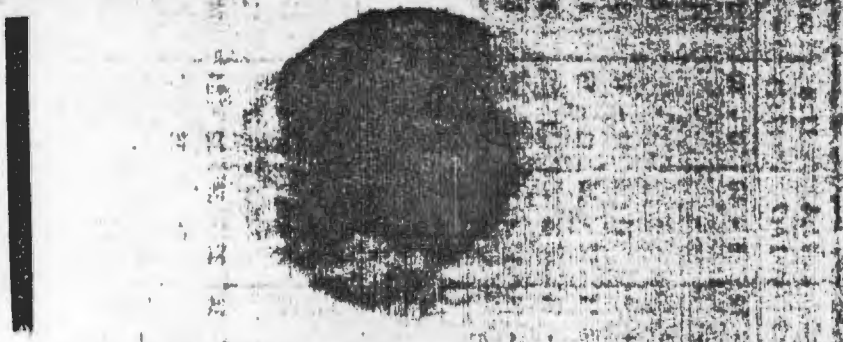
50% = 276 cnts

5% = 15 cnts

RISE TIME = 51 sec

UPBFI = 5.7

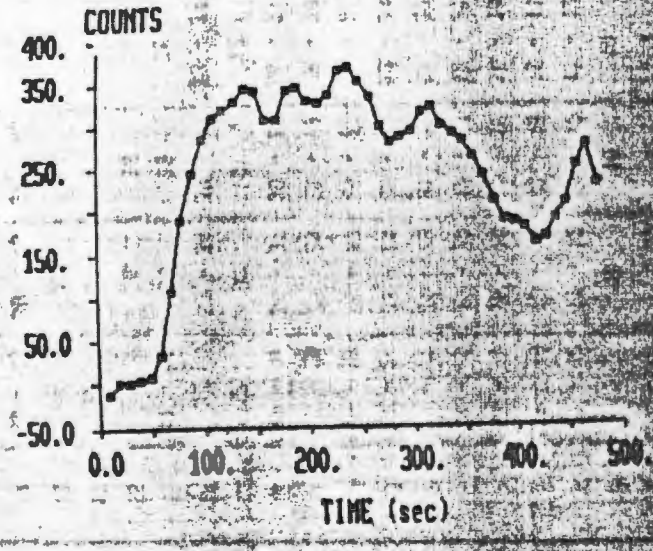
PECK,A 86/3044



#49 SUMMED IMAGES:1-48

BASELINE 2 7/23/86 9:41

BASELINE 2



PECK,A 86/3044
PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 2 7/23/86 9:41

UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 330 cnts

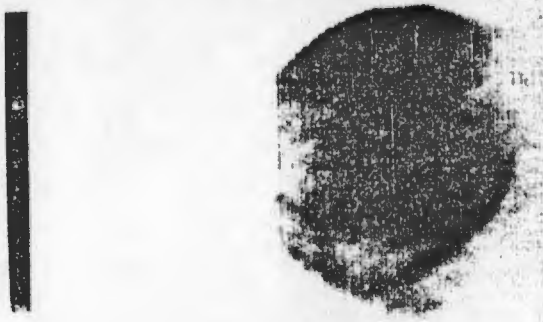
90% = 314 cnts

5% = 17 cnts

RISE TIME = 116 sec

UPBFI = ~~2.8~~ 5.5

PECK,A. 86/3044



#49 SUMMED IMAGES:1-48

POST DRUG

7/23/86 10:02

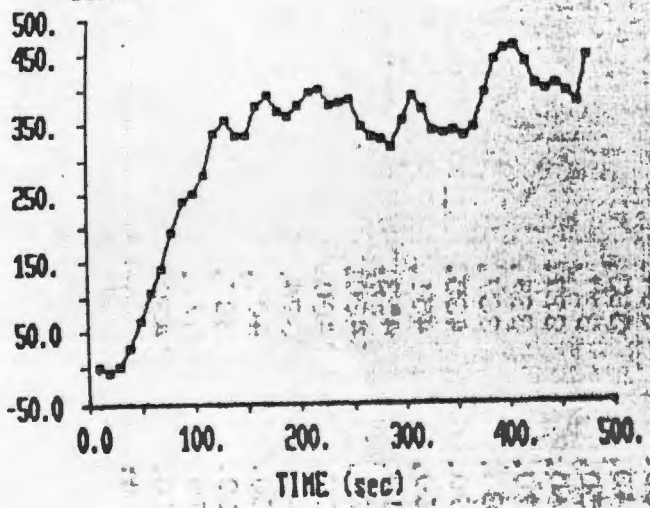
PLACENTA

#49 SUMMED IMAGES:1-48

POST DRUG

7/23/86 10:02

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 340 cnts

90% = 323 cnts

RISE TIME = 86 sec

UPBFI = 3.95

PATIENT DATA

PATIENT NO.:	5
AGE: (YRS)	32
PARITY:	2
SMOKER:	No
GESTATIONAL AGE: (WKS)	35
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	No
HAEMOGLOBIN (g%)	12.6
PLATELET COUNT:	205
URIC ACID (m mol/L)	0.31
UREA (m mol/L)	3.2
CREATININE (m mol/L)	62

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	150
	Diastolic	99
	Mean arterial pressure	116
Mean post-treatment blood pressure:	Systolic	155
	Diastolic	103
	Mean arterial pressure	121
Mean pre-treatment pulse rate		78
Mean post-treatment pulse rate		95

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	130
	Rise time	44
	Blood flow index	3.0
Pretreatment scan II	Maximum count rate	100
	Rise time	60
	Blood flow index	1.7
Post-treatment Scan	Maximum count rate	185
	Rise time	75
	Blood flow index	2.5

OCTOBER,H 86/3566

54251 392

#49 SUMMED IMAGES:1-48

8/15/86 16:07

BASELINE 1

OCTOBER,H 86/3566

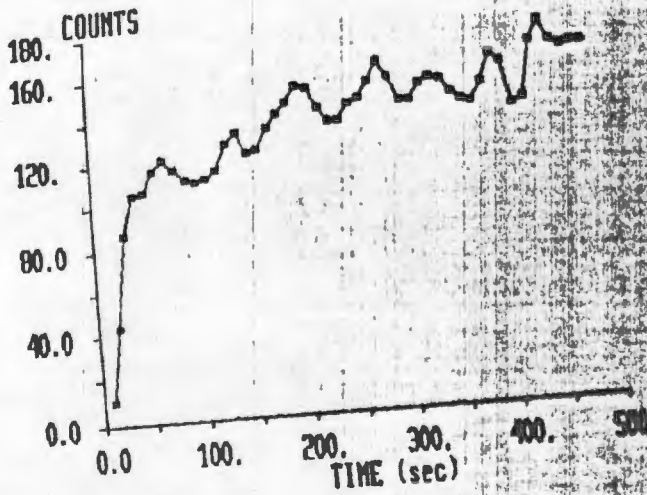
PLACENTA

#49 SUMMED IMAGES:1-48

8/15/86 16:07

BASELINE 1

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 130 cts

90% = 124 cts

5% = 7 cts

RISE TIME = 44 sec

UPBFI = 2.9

54251 392

#49 SUMMED IMAGES:1-48

BASELINE 2

8/15/86 16:57

OCTOBER,H 86/3566
PLACENTA:2

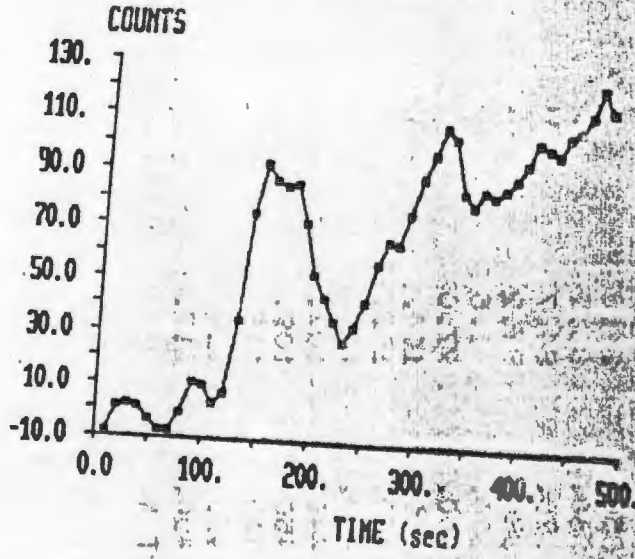
54251 392

#49 SUMMED IMAGES:1-48

BASELINE 2

8/15/86 16:57

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 100 cts

95% = 95 cts

5% = 5 cts

RISE TIME = 60 sec

UFBFI = 1.7

UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 185 cts

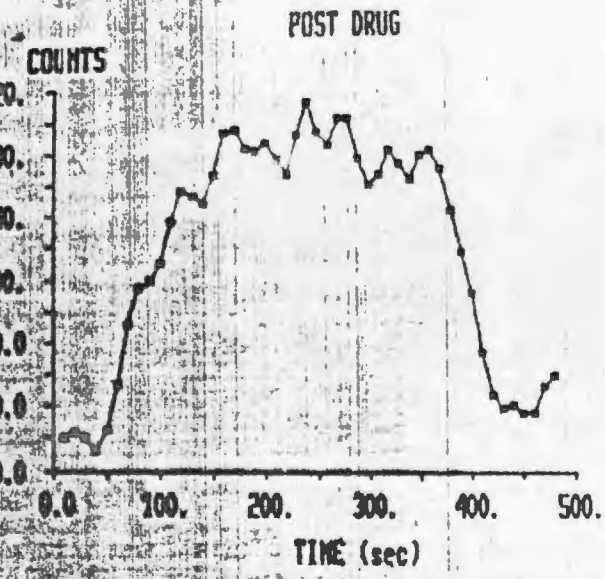
96% = 176 cts

5% = 9 cts

RISE TIME = 44 sec

UPBFI = 2.35

POST DRUG 8/15/86 17:15



PATIENT DATA

PATIENT NO.:	6
AGE: (YRS)	27
PARITY:	1
SMOKER:	No
GESTATIONAL AGE: (WKS)	38
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	No
HAEMOGLOBIN (g%)	12.2
PLATELET COUNT:	209
URIC ACID (m mol/L)	0.25
UREA (m mol/L)	2.3
CREATININE (m mol/L)	62

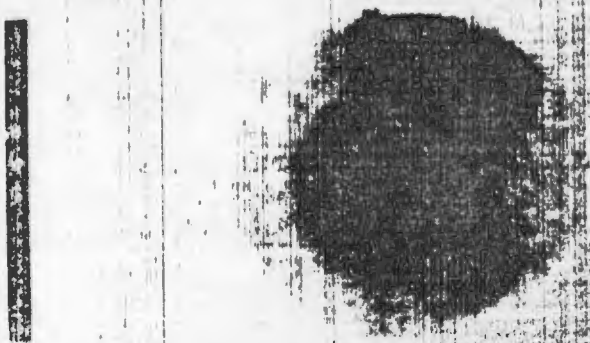
1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	158
	Diastolic	109
	Mean arterial pressure	123
Mean post-treatment blood pressure:	Systolic	156
	Diastolic	109
	Mean arterial pressure	123
Mean pre-treatment pulse rate		85
Mean post-treatment pulse rate		93

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	270
	Rise time	120
	Blood flow index	2.3
Pretreatment scan II	Maximum count rate	250
	Rise time	102
	Blood flow index	2.5
Post-treatment Scan	Maximum count rate	360
	Rise time	99
	Blood flow index	3.6

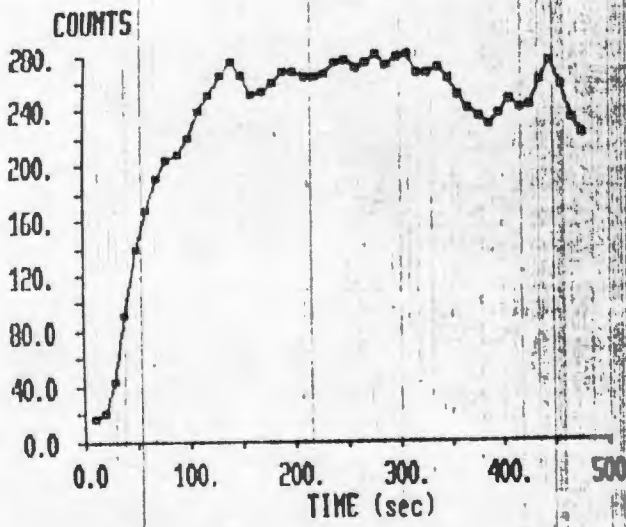
HAAS,J 86/3567 61351 730



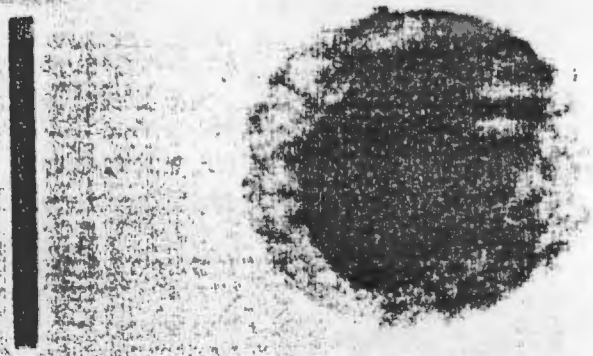
1-48 SUMMED IMAGES 1-48

BASELINE 1 8/16/86 9:47

BASELINE 1



HAAS,J 86/3567 61351 730
PLACENTA



1-48 SUMMED IMAGES 1-48

BASELINE 1 8/16/86 9:47

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 270 cnts

95% = 258 cnts

5% = 14 cnts

RISE TIME = 120 sec

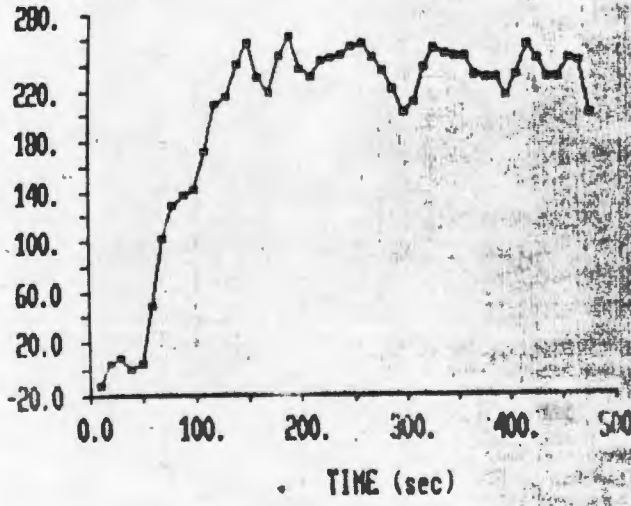
UPBFI = 2.25

HAAS,J 86/3567 61351 730

#49 SUMMED IMAGES:1-40

BASELINE 2 8/16/86 10:12

BASELINE 2



HAAS,J 86/3567 61351 730
PLACENTA

#43 SUMMED IMAGES:1-40

BASELINE 2 8/16/86 10:12

UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 250 cnts

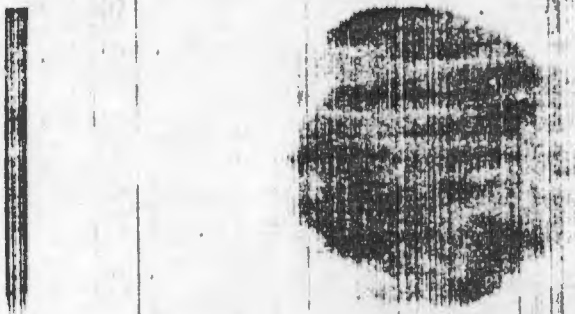
95% = 238 cnts

5% = 13 cnts

RISE TIME = 102 sec

UPOFI = 2.45

HAYS,J 86/3567 61351 730



#49 SUMMED IMAGES:1-48

POST DRUG 8/16/86 10:32

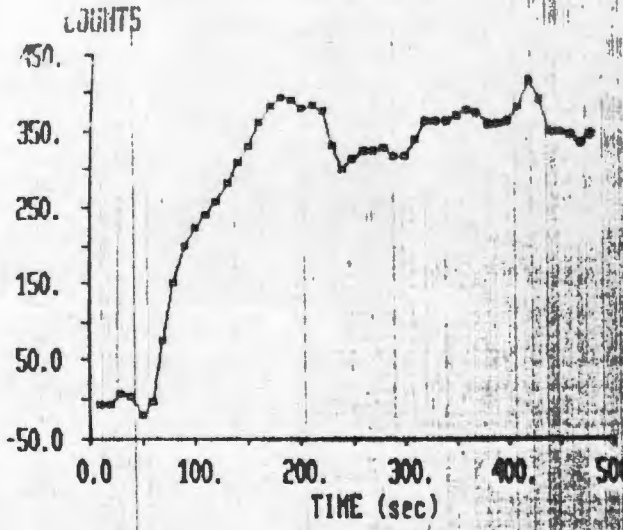
HAYS,J 86/3567 61351 730

PLACENTA

#49 SUMMED IMAGES:1-48

POST DRUG 8/16/86 10:32

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 360 cnts

95% = 342 cnts

5% = 18 cnts

RISE TIME = 99 sec

UPBFI = 3.6

PATIENT DATA

PATIENT NO.:	7
AGE: (YRS)	25
PARITY:	2
SMOKER:	No
GESTATIONAL AGE: (WKS)	34
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	1.6 g/24 hrs
HAEMOGLOBIN (g%)	15
PLATELET COUNT:	261
URIC ACID (m mol/L)	0.41
UREA (m mol/L)	2.9
CREATININE (m mol/L)	53

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	154
	Diastolic	113
	Mean arterial pressure	127
Mean post-treatment blood pressure:	Systolic	150
	Diastolic	105
	Mean arterial pressure	120
Mean pre-treatment pulse rate		87
Mean post-treatment pulse rate		107

2. BLOOD FLOW INDICES:

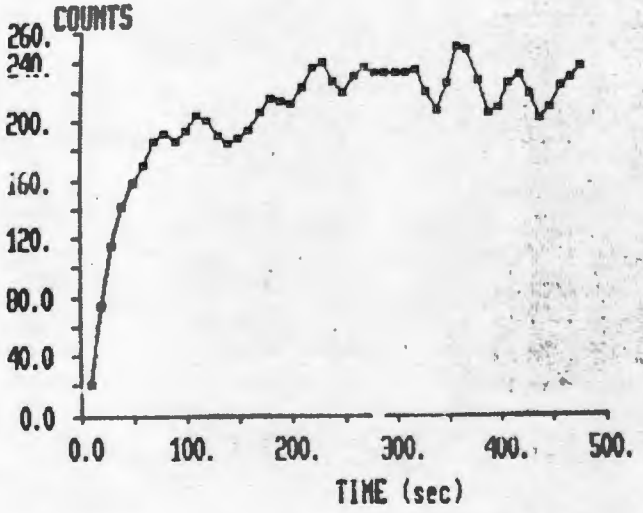
Pretreatment scan I	Maximum count rate	205
	Rise time	70
	Blood flow index	2.9
Pretreatment scan II	Maximum count rate	195
	Rise time	51
	Blood flow index	3.8
Post-treatment Scan	Maximum count rate	225
	Rise time	70
	Blood flow index	3.2

VAN REMSBURG,J 86/3102 68598 978

#49 SUMMED IMAGES 1-48

BASELINE 1 7/27/86 10:36

BASELINE 1



VAN REMSBURG,J 86/3102 68598 978

PLACENTA

#49 SUMMED IMAGES 1-48

BASELINE 1 7/27/86 10:36

UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 205

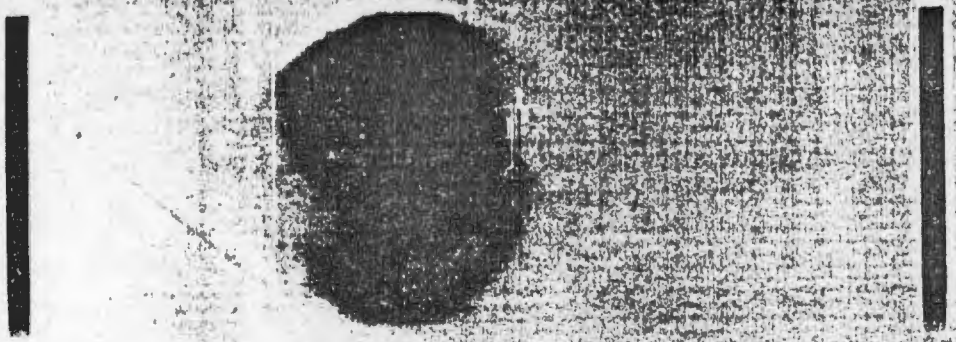
90% = 195

5% = 10

RISE TIME = 70 sec

UPBFI = 2.9

VAN RENSBURG,J 86/3102 GE930 978



#49 SUMMED IMAGES 1-48

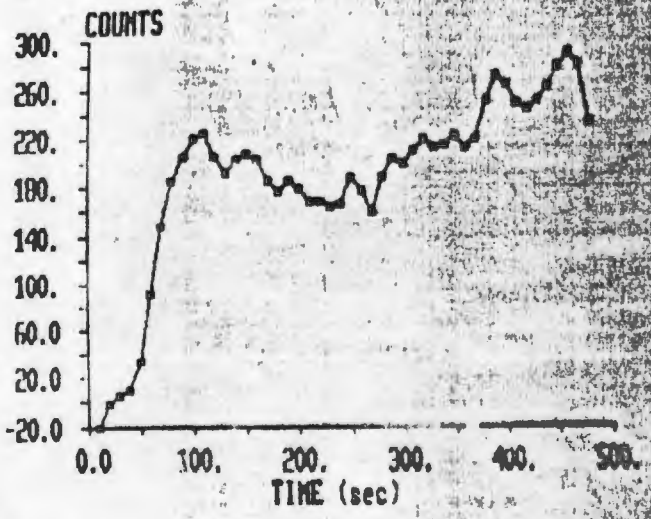
BASELINE 2 7/27/86 11:20

VAN RENSBURG,J 86/3102 GE930 978
PLACENTA

#49 SUMMED IMAGES 1-48

BASELINE 2 7/27/86 11:20

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 195

90% = 185

5% = 10

RISE TIME = 51 sec

UPSLI = 3.8

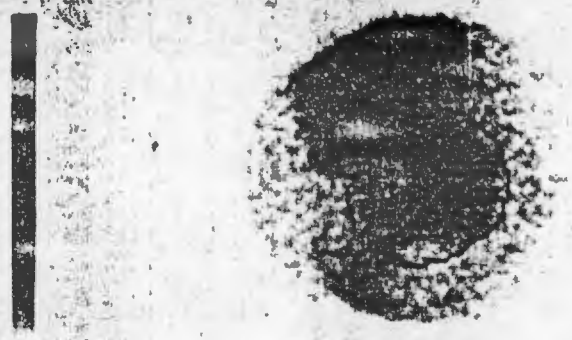
VAN REMSBURG,J 86/3102 68598 978

#49 SUMMED IMAGES 1-48

POST DRUG 7/27/86 11:59

VAN REMSBURG,J 86/3102 68598 978

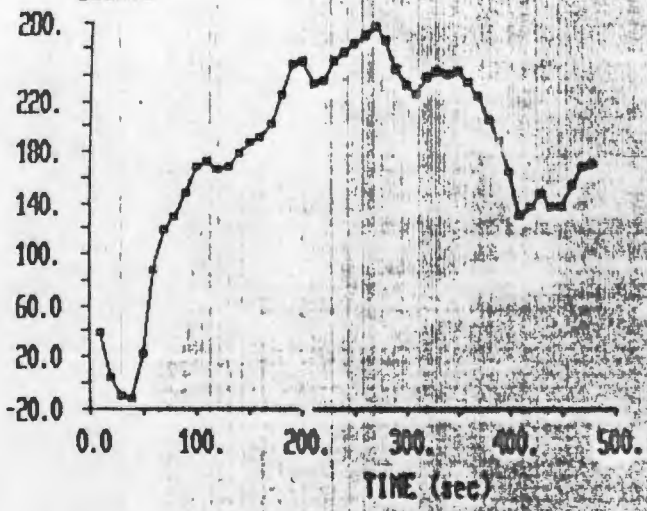
PLACENTA



#49 SUMMED IMAGES 1-48

POST DRUG 7/27/86 11:59

POST DRUG



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 225 cnts

90% = 214 cnts

RISE TIME = 70 sec

UPBFI = 3.2

PATIENT DATA

PATIENT NO.:	8
AGE: (YRS)	33
PARITY:	5
SMOKER:	No
GESTATIONAL AGE: (WKS)	32
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	1.4 g/24 hrs
HAEMOGLOBIN (g%)	14.7
PLATELET COUNT:	275
URIC ACID (m mol/L)	0.48
UREA (m mol/L)	3.9
CREATININE (m mol/L)	70

1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	149
	Diastolic	107
	Mean arterial pressure	120
Mean post-treatment blood pressure:	Systolic	133
	Diastolic	99
	Mean arterial pressure	110
Mean pre-treatment pulse rate		63
Mean post-treatment pulse rate		85

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	140
	Rise time	150
	Blood flow index	0.9
Pretreatment scan II	Maximum count rate	185
	Rise time	144
	Blood flow index	1.3
Post-treatment Scan	Maximum count rate	!80
	Rise time	92
	Blood flow index	2.0

AJAM,F 86/3893 52260 320

#49 SUMMED IMAGES:1-48

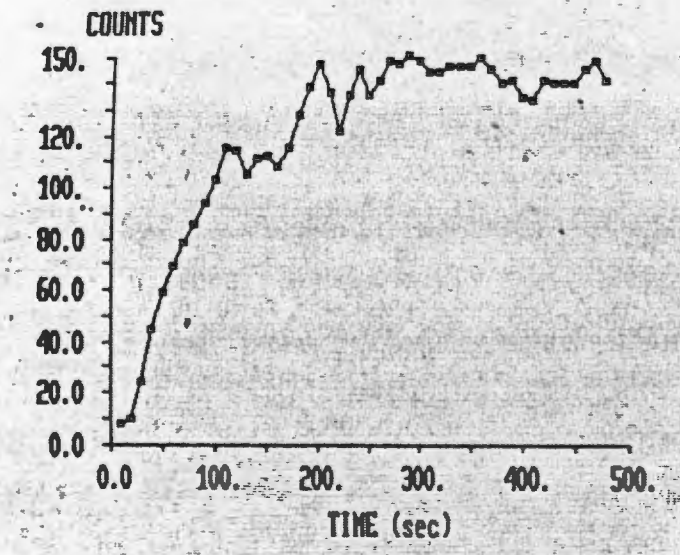
BASELINE 1 9/12/86 8:57

AJAM,F 86/3893 52260 320
PLACENTA

#49 SUMMED IMAGES:1-48

BASELINE 1 9/12/86 8:57

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100% = 140 cnts

95% = 133 cnts

5% = 7 cnts

RISE TIME = 150 sec

UPBFI = 0.9

AJAM,F 86/3893 S2260 320

IMAGE #1

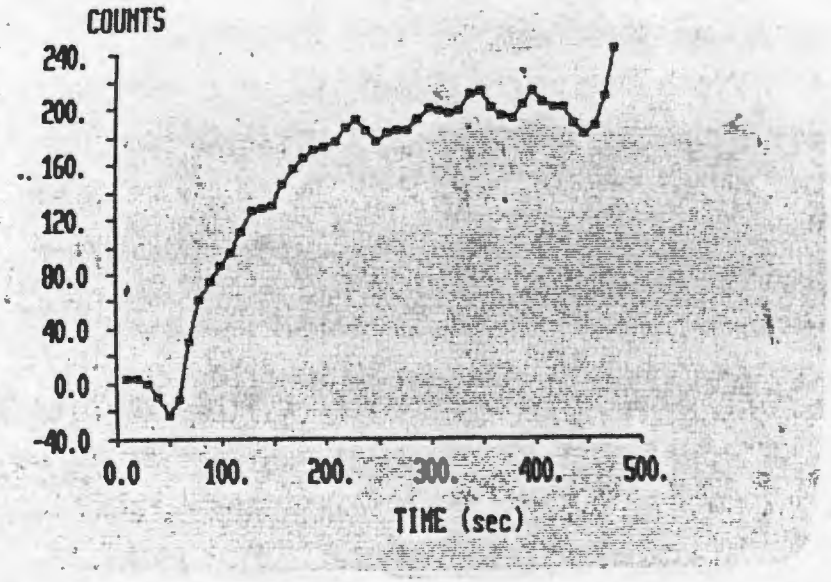
BASELINE 2 9/12/86 9:26

AJAM,F 86/3893
PLACENTA 2

IMAGE #1

BASELINE 2 9/12/86 9:26

BASELINE 2



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 185 cnts

95% = 176 cnts

5% = 9 cnts

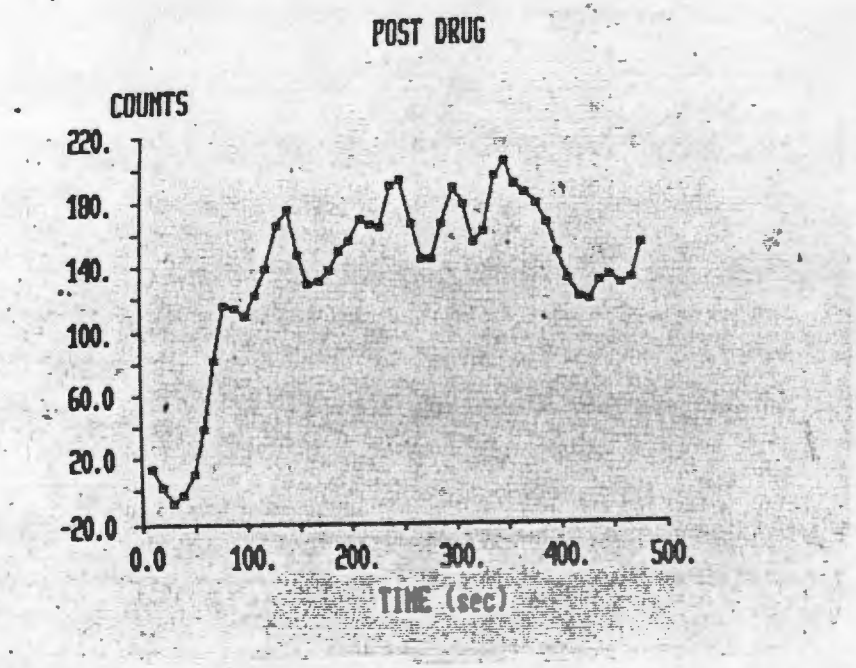
RISE TIME = 144 sec

UPBFI = 1.3

AJAM,F 86/3893 52260 320

#49 SUMMED IMAGES:1-48

POST DRUG 9/12/86 10:01



AJAM,F 86/3893 52260 320
PLACENTA 2

#49 SUMMED IMAGES:1-48

POST DRUG 9/12/86 10:01

UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 180 cnts

95% = 171 cnts

5% = 9 cnts

RISE TIME = 92 sec

UPBFI = 1.95

PATIENT DATA

PATIENT NO.:	9
AGE: (YRS)	24
PARITY:	1
SMOKER:	No
GESTATIONAL AGE: (WKS)	41
PLACEBO/MEDICINE:	Nifedipine
PROTEINURIA:	0.38 g/24 hrs
HAEMOGLOBIN (g%)	13.8
PLATELET COUNT:	332
URIC ACID (m mol/L)	0.38
UREA (m mol/L)	3.2
CREATININE (m mol/L)	62

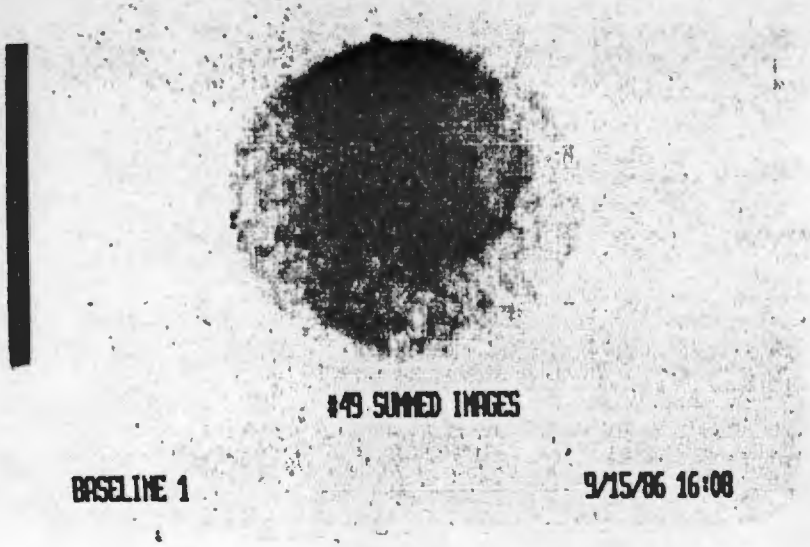
1. BLOOD PRESSURE INDICES:

Mean pre-treatment blood pressure:	Systolic	138
	Diastolic	98
	Mean arterial pressure	110
Mean post-treatment blood pressure:	Systolic	128
	Diastolic	91
	Mean arterial pressure	101
Mean pre-treatment pulse rate		78
Mean post-treatment pulse rate		87

2. BLOOD FLOW INDICES:

Pretreatment scan I	Maximum count rate	120
	Rise time	74
	Blood flow index	1.6
Pretreatment scan II	Maximum count rate	125
	Rise time	68
	Blood flow index	1.8
Post-treatment Scan	Maximum count rate	205
	Rise time	112
	Blood flow index	1.8

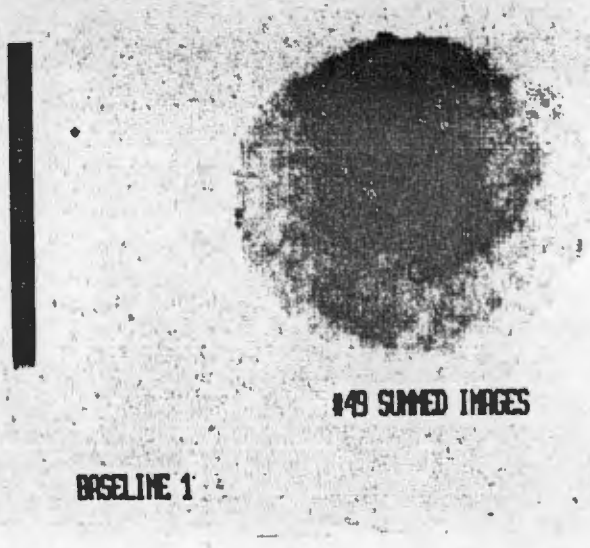
SMART,L 86/3933 68635 564



#49 SUMMED IMAGES

BASELINE 1 9/15/86 16:08

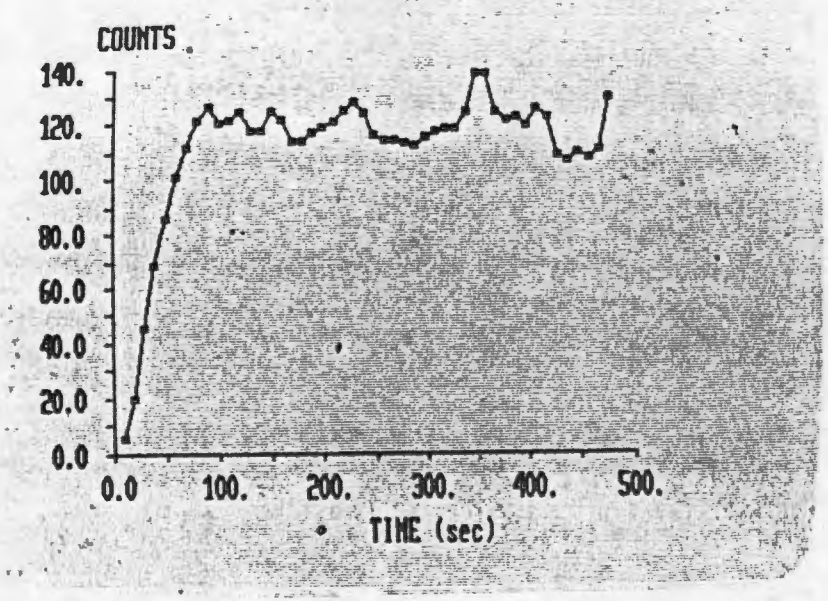
SMART,L 86/3933 68635 564
PLACENTAL ROI



#49 SUMMED IMAGES

BASELINE 1 9/15/86 16:08

BASELINE 1



UTERO-PLACENTAL BLOOD FLOW

BASELINE 1

100 % = 120 cnts

95 % = 114 cnts

5 % = 6 cnts

RISE TIME = 74 sec

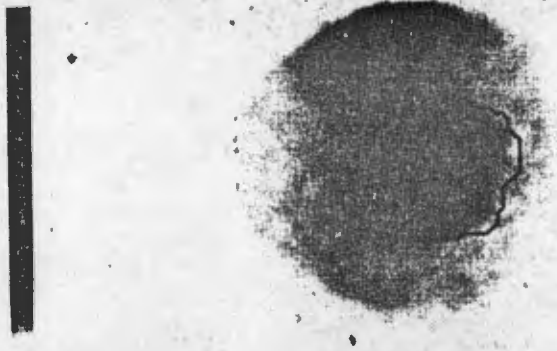
UPBFI = 1.62

SHART,L 86/3933 68635 564

#49 SUMMED IMAGES:1-48

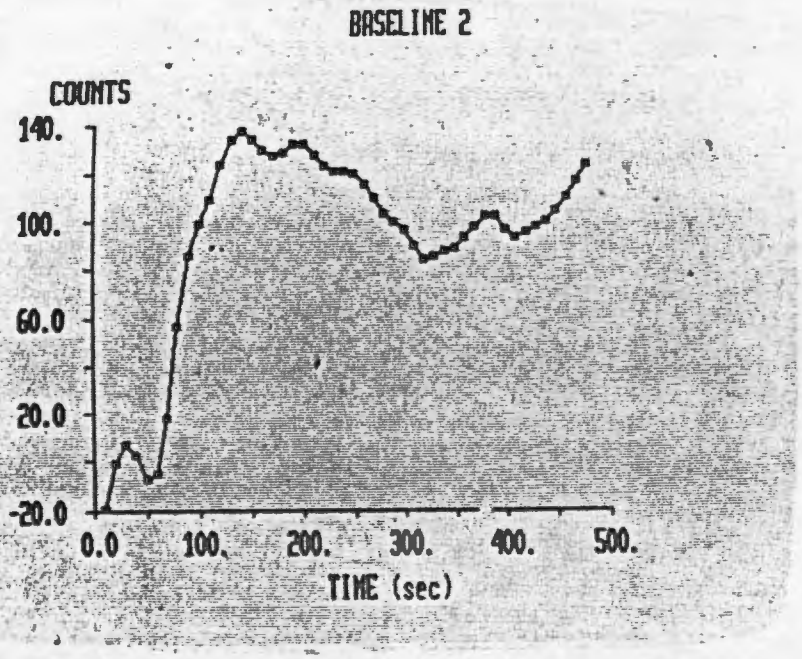
BASELINE 2 9/15/86 17:04

SHART,L 86/3933 68635 564
PLACENTA



#49 SUMMED IMAGES:1-48

BASELINE 2 9/15/86 17:04



UTERO-PLACENTAL BLOOD FLOW

BASELINE 2

100% = 125 cnts

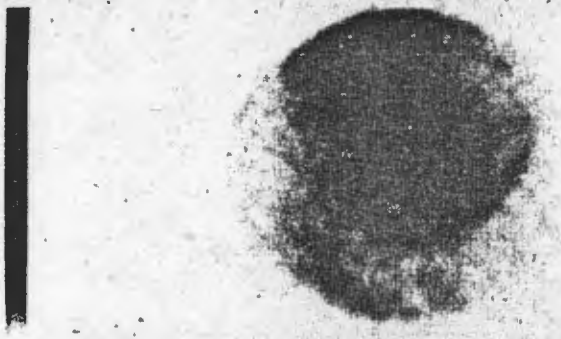
95% = 119 cnts

5% = 6 cnts

RISE TIME = 6 sec

UPBFI = 1.8

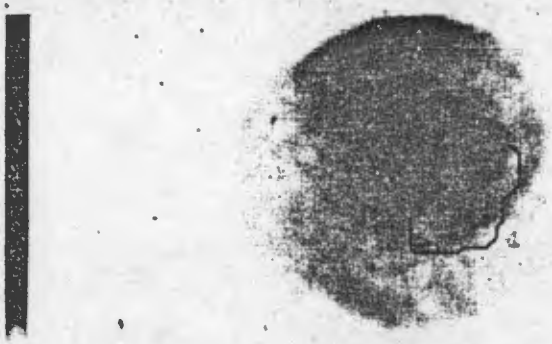
SHART,L 86/3933 68635 564



#49 SUMMED IMAGES:1-48

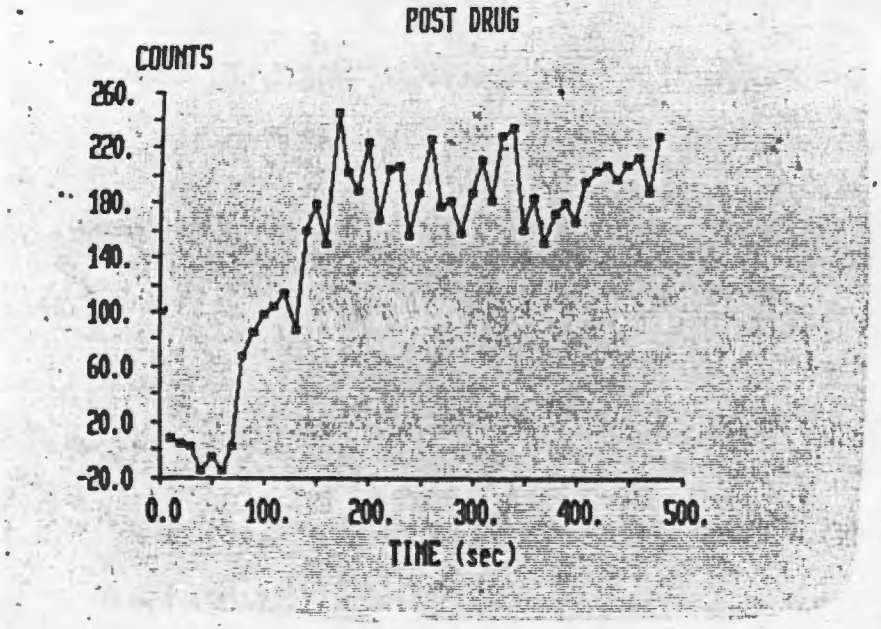
POST DRUG 9/15/86 17:37

SHART,L 86/3933 68635 564
PLACENTA



#49 SUMMED IMAGES:1-48

POST DRUG 9/15/86 17:37



UTERO-PLACENTAL BLOOD FLOW

POST DRUG

100% = 205 cnts

95% = 195 cnts

5% = 10 cnts

RISE TIME = 112 sec

UPBFI = 1.8

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