Blood Flow Measurements

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76.1 Doppler Measurements

Ultrasound Doppler

The ultrasound Doppler measurements [1, 2] are based on a principle discovered by the Austrian physicist Christian Doppler 1842 [3], who theoretically predicted that a wave, backscattered from a moving object, will be shifted in frequency. The principle was verified by two hornblowers, one aboard a moving train and the other standing still, with the ability to assess the pitch of the sound.

To obtain a Doppler signal from a fluid, the fluid must contain scattering particles, which in the case of blood are the blood cells. The size of a red blood cell is about 2×7 μm, which means that the scatterers are much smaller than the wavelength of the ultrasound. Hence, a diffuse scattering of the ultrasound will occur (Rayleigh scattering). The scattering from tissues surrounding the heart and vessels usually gives a much larger signal (20 to 40 dB) than that from blood in motion. The velocity of tissue motion is usually much lower than that of blood. This contribution can therefore be suppressed by high-pass filtering. In recent years ultrasound contrast agents (consisting of gas-filled shells) have been introduced to increase the blood flow signal. Figure 76.1 illustrates the ultrasound Doppler principle. An ultrasound beam is sent toward a moving object. The beam hits the object and returns to the receiver with a Doppler-shifted frequency carrying information about the velocity of the object.

The Doppler shift f_d of an ultrasound signal with the nominal frequency f_c is given by

$$f_d = 2 f_c \cdot \frac{v}{c} \tag{76.1}$$

where v is the velocity component in the direction of the ultrasound beam and c is the speed of sound in the medium which is in the range of 1500 to 1600 m s^{-1} in soft tissue and usually set to 1540 m s^{-1}. The frequency f_c is in the range of 2 to 10 MHz, which gives a wavelength between 0.15 and 0.77 mm.

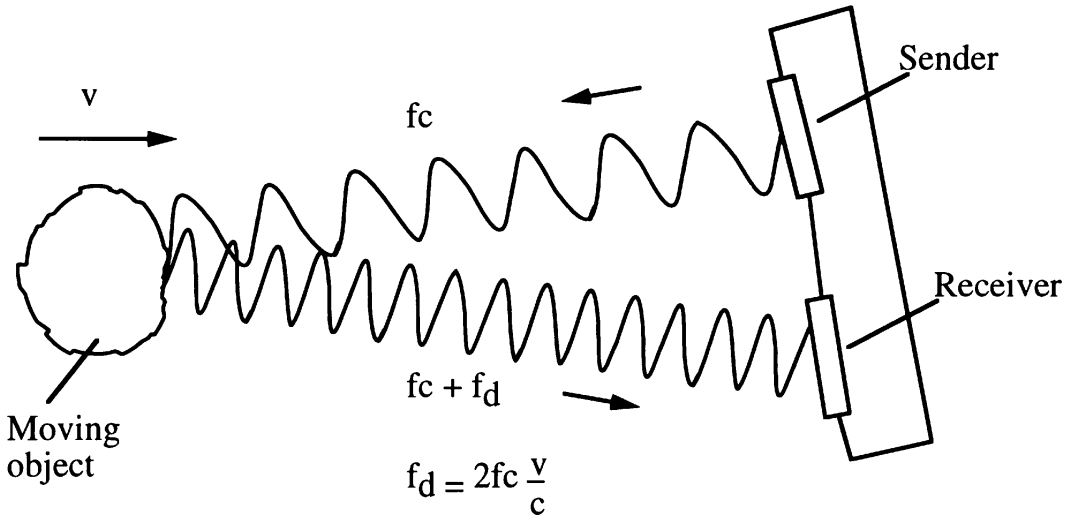

FIGURE 76.1 For Doppler ultrasound, the moving object shifts the received frequency.

The peak systolic flow velocity in the heart and larger vessels is normally 0.5 to 1 m s^{-1}, resulting in a Doppler shift in the range of 1.3 to 13 kHz (depending on the ultrasound frequency f_c). The Doppler sound is therefore audible, which is helpful for the investigator in identifying vessels and phenomena of interest.

The most straightforward ultrasound investigation is to use a continuous wave system. The ultrasound beam is focused by a suitable ultrasound transducer geometry and by a lens. By this arrangement a narrow beam can be arranged and the backscattered information can come from any section along the beam.

In order to know from where along the beam the blood flow data are collected, a pulsed Doppler system has to be used. The transducer sends four to eight cycles of the ultrasound signal; a specified time later a gate is opened and the transducer will act as a reviewer. By using a preset time delay between the sending and the reviewing signal only flow information from a certain depth will be collected. The depth is obviously determined by the delay time and the propagation velocity in the tissue. Flow velocity information is obtained by spectral estimation of the Doppler signal.

By multirange gating, blood flow at various points along the ultrasound beam can be measured. By scanning with an ultrasound beam within a sector, a two-dimensional velocity field can be presented. By color coding the information a color Doppler flow image can be obtained. By scanning in one additional orthogonal plane, a three-dimensional flow image can be created.

An important medical application of the ultrasound Doppler is in the study of heart valve flow when one might suspect stenosis or leaking flow in the valves. The pumping ability of the heart can be assessed from the general flow patterns. Regions with arteriosclerotic obstructions can be localized in the peripheral vessels.

Laser Doppler Flowmetry

The Doppler principle is also utilized in blood flow measurements in the microcirculatory bed in which laser Doppler flowmetry measures the blood perfusion. Laser light from a gas or semiconductor laser is launched into an optical fiber which leads the light to the tissue. (Figure 76.2). Photons are reflected, scattered, and absorbed in the tissue matrix and those that hit moving red blood cells become Doppler shifted, whereas those that are reflected in stationary structures are refracted without any change in frequency. A part of the photons returning to the fiber-optic system will be conducted by the pickup fiber to the detector. Shifted and nonshifted photons are mixed at the surface of a square-law photodetector. According to elementary wave mechanics this type of mixing (coherent detection) results in the

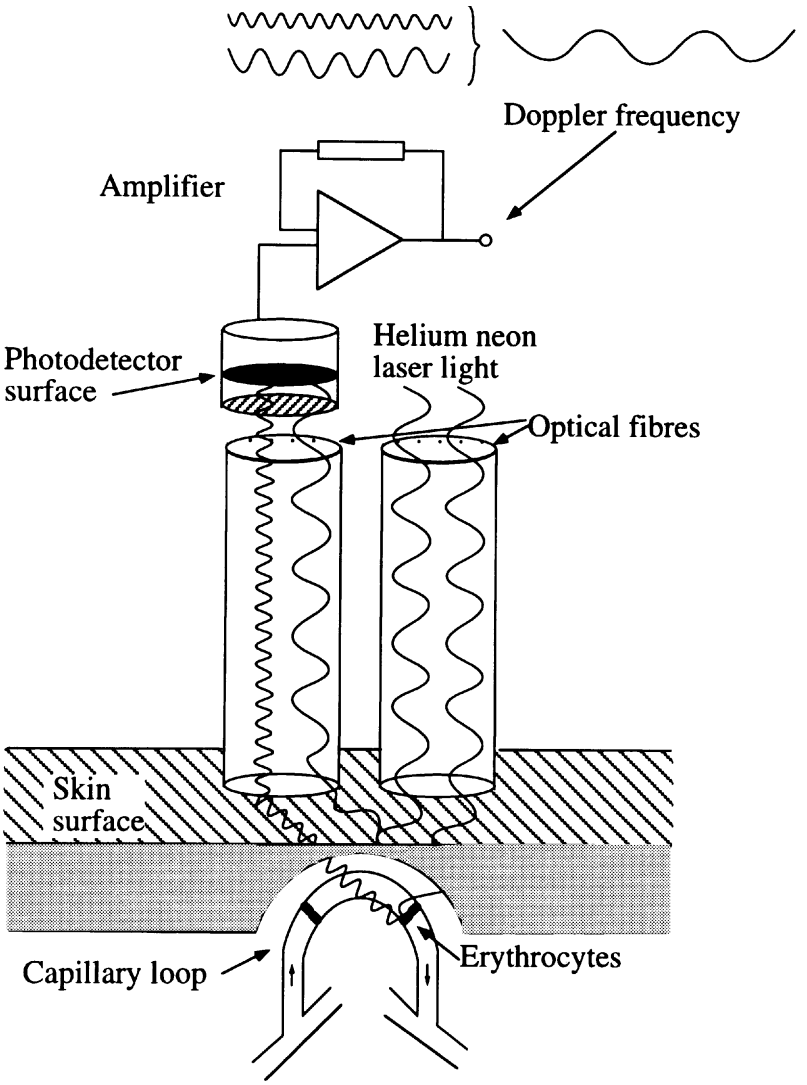

FIGURE 76.2 For laser Doppler flowmetry, the moving blood cells shift the received frequency.

sum and difference frequencies. The frequency of the "difference wave" is proportional to the average velocity of the red blood cells. The amplitude of the same signal is proportional to the number of moving scatterers in the tissue volume. A velocity distribution will result in a Doppler spectrum, usually in the range of 30 to 12,000 Hz.

Variants of the method utilizing fiber optics, airborne beams, microscope-based setups, and color-coded imaging scanners are described in the literature. For a review, see Shepherd and Öberg [4].

76.2 Indicator Dilution Methods

Cardiac output measurement is one of the most essential heart performance measures. The rest and exercise flows carry important diagnostic information. The monitoring of cardiac output is very important for the critically ill patient.

The principle is that an indicator is injected upstream in the circulation. Mixing with the circulating blood volume occurs and the indicator concentration is detected downstream. By knowing the added

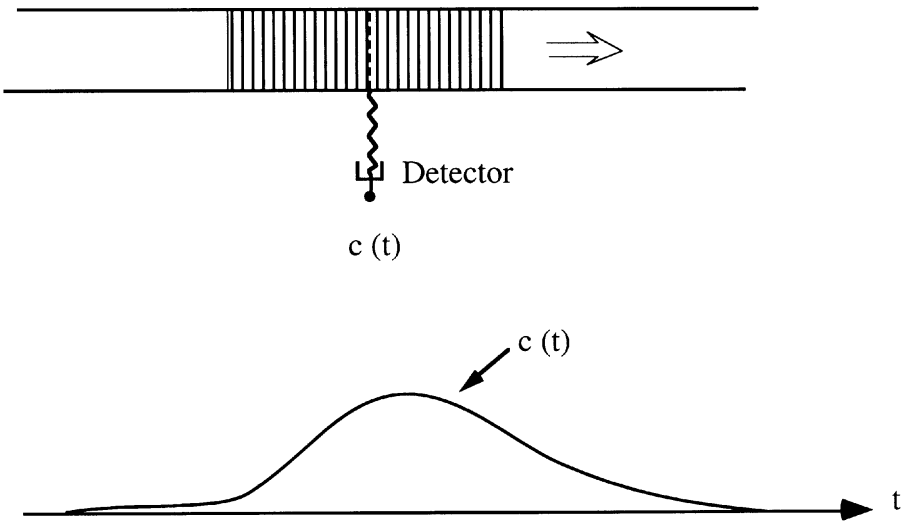

FIGURE 76.3 Indicator dilution measurements. The flow can be calculated if the amount of indicator and the time course of its concentration are known.

quantity of indicator and the time integral of the detected indicator concentration, the flow can be determined (Figure 76.3).

We can subdivide the indicator dilution methods into dye dilution and thermal dilution methods. See Webster [5] and Bronzino [6].

Dye Dilution Method

To determine the cardiac output (l/min) a known quantity (mass m) of a dye indicator such as Evans Blue is injected into the right heart and a concentration of the indicator $c(t)$ is detected in the pulmonary artery. At the time t an indicator quantity Δm passes the detector at a time interval Δt. If F is the blood flow,

$$\Delta m = F\, c\left(t\right)\Delta t \tag{76.2}$$

or by integration

$$F = \frac{m}{\int c\left(t\right)dt} \tag{76.3}$$

Thus, only the amount of indicator added and the time integral of the downstream concentration, assuming good mixing, has to be known to be able to calculate the flow, i.e., the cardiac output.

Thermal Dilution Method

The thermal dilution method is a variant of the indicator dilution method family. A thermal dilution catheter is placed with the injection outlet in the right atrium of the heart and with a temperature sensor in the pulmonary artery (Bronzino [6] and Weissel et al. [7]).

A chilled solution of dextrose in water or saline solution is used for the injection and causes transient decrease in the pulmonary artery temperature $T(t)$. The blood flow (cardiac output) can be calculated from

$$F = \int T(t)dt\rho_b c_b = V(T_b - T_i)\rho_i c_i K \tag{76.4}$$

or

$$F = \frac{V(T_b - T_i)}{\int T(t)dt}\left(\rho_i c_i / \rho_b c_b\right)K \tag{76.5}$$

where V is the injected volume, T_b the undisturbed temperature in the pulmonary artery, T_i the temperature of the indicator, r_i and r_b the density of the indicator and the blood, c_i and c_b the specific heat of the indicator and the blood and K is a correction factor that takes heat transfer along the catheter into account.

The thermodilution technique is the standard technique for the monitoring of cardiac output in critically ill patients.

76.3 Plethysmography

The word *plethysmography* means methods for recording volume changes of an organ or a body part. Depending on the technique used, strain gage, impedance, and optical techniques can be used for the volume determination. See Webster [5] and Figure 76.4.

Strain Gage Plethysmography

The classical strain gage plethysmography is used to study circulation in the lower extremities from changes in the circumference of the legs.

Small-diameter silicone rubber tubes, filled with mercury or other types of conductive liquids, are placed around the circumference of the leg. Changes in the latter can be directly related to electrical impedance changes of the silicone rubber tube. If a cylindrical cross section of the leg is assumed, volume changes should be proportional to the total circumference, times the change in impedance.

The strain gage tubes (Figure 76.4) are positioned around the lower part of the leg, an inflatable cuff is placed around the upper part (above the knee) and inflated to 40 to 50 mmHg, i.e., above the venous pressure that will cause the outflow of blood to cease. The increased volume of the leg is therefore proportional to the arterial inflow. The latter is determined from the initial slope. Flow is volume increase per time unit.

When the cuff pressure is released, blood will flow out from the leg via the veins. The time course of the volume change will be related to venous function. If there is venous thrombosis, the decline in the volume curve will be slower.

Impedance Plethysmography

Bioelectric impedance measurements have a history dating back to the 1940s. The reason impedance is useful for detection of volume changes is that different tissues in the body have different resistivity. Blood is one of the best conductors among the tissues of the body.

Impedance plethysmography has its most established applications in respiratory monitoring in newborn infants and for detection of venous thrombosis. Less-established applications are cardiac output measurements, peripheral blood flow studies, and body composition assessments.

A constant current with a frequency of 50 to 100 kHz and an amplitude of 0.5 to 4 mA rms is applied via skin electrodes (Figure 76.4). Influences from skin impedance are eliminated by the use of the four electrode technique.

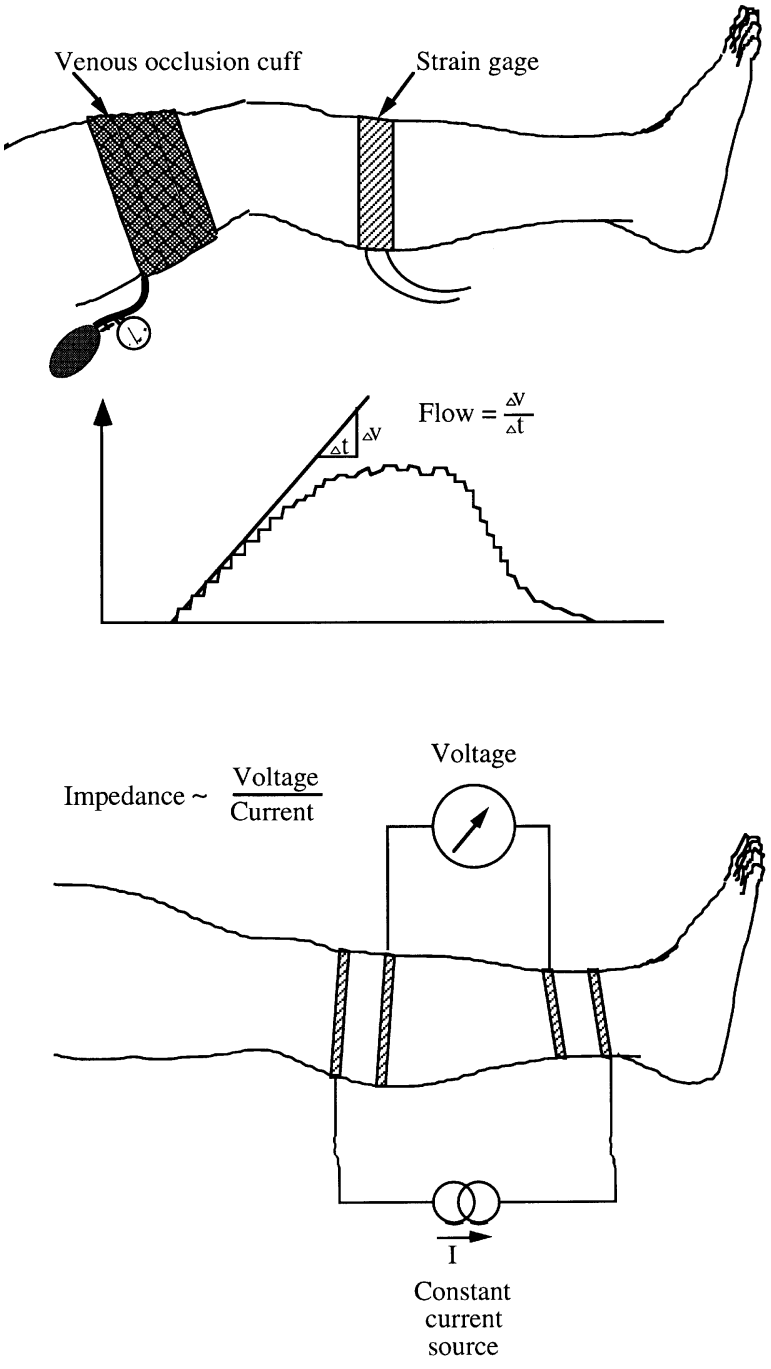

FIGURE 76.4 For occlusion plethysmography, increased volume stretches the strain gage (top) and decreases the impedance (bottom).

The measurement object can be described with a conduction object with the constant impedance Z_o in parallel with a time-varying impedance ΔZ. The impedance ΔZ is represented with a column of a conducting media with resistivity ρ and the length L. If the changes in ΔZ are small in comparison to those of Z_o, the volume changes can be obtained as:

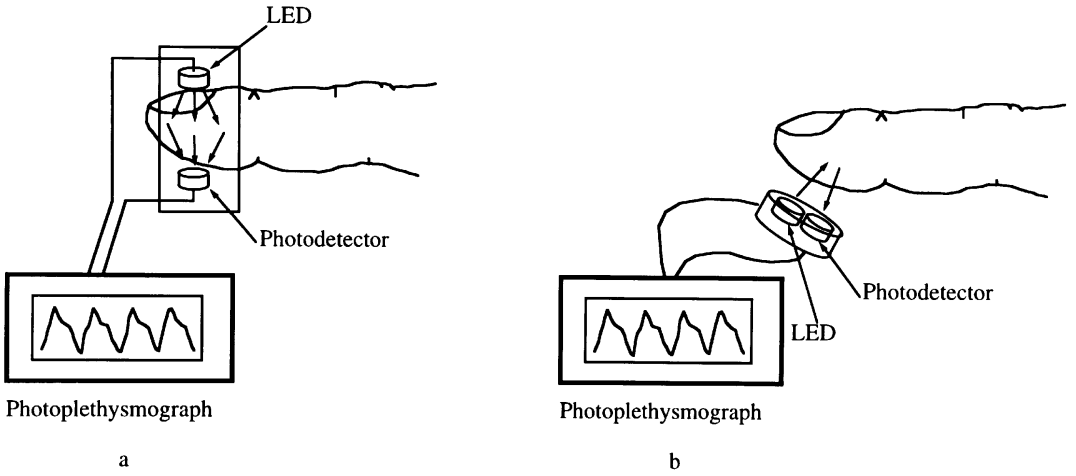

FIGURE 76.5 For photoplethysmography, increased blood decreases received light in (a) transmission mode and (b) reflection mode.

$$\Delta V \approx \rho \frac{L^2}{Z_0^2} \Delta Z \tag{76.6}$$

This technique can be used in the same way as the strain gage plethysmoghraphic method to study circulation in the leg.

For the measurement of cardiac output, Equation 76.6 or a modified formula can be used [8]. The method seems to work rather well in normal persons for relative change, but for patients with cardiac disease the cardiac output estimation might be poor.

Photoelectric Plethysmography

Hertzman and Spealman [9] and Hertzman [10] were the first to use the descriptive term *photoelectric plethysmography* (PPG). The first reports on the successful use of the principle were published in the middle of 1930 by Molitor and Kniazuk [11]. The principle on which PPG is based is simple, although the underlying detailed optical mechanisms remain unknown. A beam of light is directed toward the part of the tissue in which blood flow (or volume) is going to be measured. (Figure 76.5). Reflected, transmitted, and scattered light leaving this volume is collected and focused on a photodetector. A signal modulated by the attenuation or scattering of light in the blood volume can be recorded. Two different components can be derived from the detector. One is pulsatile and synchronous with the heartbeat (the ac component), the other is a constant voltage (the dc component). The physiological significance of the two signals is still under debate, but they reflected the blood volume and the orientation of erythrocytes during the cardiac cycle.

PPG has been used mainly for monitoring blood perfusion in skin, venous reflux conditions, and skin flaps during plastic surgery. Challoner [12], Roberts [13], and Bernstein [14] have reviewed the methodology and applications of PPG.

76.4 Radioisotopes

Kety [15] introduced the principle of tissue clearance of rapidly diffusing inert isotopes for blood flow measurements. An extensive theoretical treatment is given by Zierler [16]. In most applications, lipid-soluble gases like ^{133}Xe and ^{85}Kr have been used. These isotopes rapidly diffuse from blood to tissue and

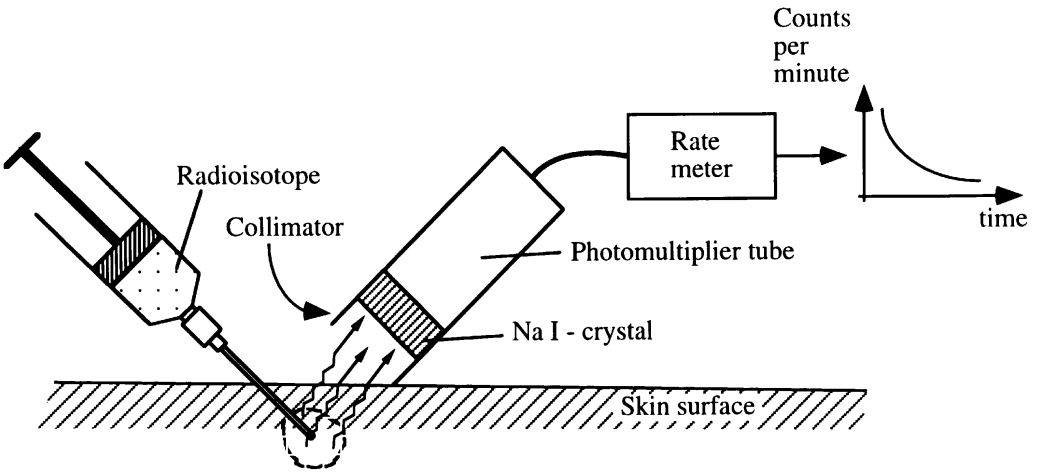

FIGURE 76.6 For isotope measurement of microcirculatory blood flow, radioactivity decreases with washout.

a rapid equilibration of the isotope concentration within a tissue volume takes place. Figure 76.6 illustrates the measurement principle. Their elimination from a microcirculatory bed is related to the blood flow rate. If the tissue is uniformly and constantly perfused, the activity of the isotope decays monoexponentially with time. The elimination of the isotope can be described by the equation

$$C(t) = C_0 \exp(-kt) \tag{76.7}$$

where $C(t)$ and C_0 are the tissue concentrations at times t and at the onset of the injection C_0. k is the clearance constant related to the local blood flow by the relation

$$k = \ln 2 / t_{1/2} \tag{76.8}$$

in which $t_{1/2}$ is half the time of decay. Blood flow Q (in $k \cdot s \cdot 100$ ml $\cdot$ min$^{-1} \cdot 100$ g^{-1}) can then be derived from the formula

$$Q = k \cdot s \cdot 100 \tag{76.9}$$

where s denotes the tissue–blood partition coefficient. The indicator is administered via an injection into the tissue volume, or through passive diffusion after deposition on the surface of the tissue volume under study.

The advantage of clearance methods is that they can be applied to the study of all kinds of tissue blood flow problems. One of the disadvantages is that the method does not give a continuous measurement of flow. In addition, the clearance curves are sometimes difficult to interpret. The trauma caused by injection of the isotope into the tissue seriously disturbs the flow, as shown by Holloway [17] and Sejrsen [18]. In spite of these shortcomings, the isotope clearance method has been applied extensively to the study of skin and tissue blood flow in experimental as well as clinical problem areas.

76.5 Thermal Convection Probes

Thermal convection probes have been developed specifically for skin blood flow measurements. Gibbs [19] pioneered the field by describing a probe in the form of a needle. Hensel and Bender [20] and van

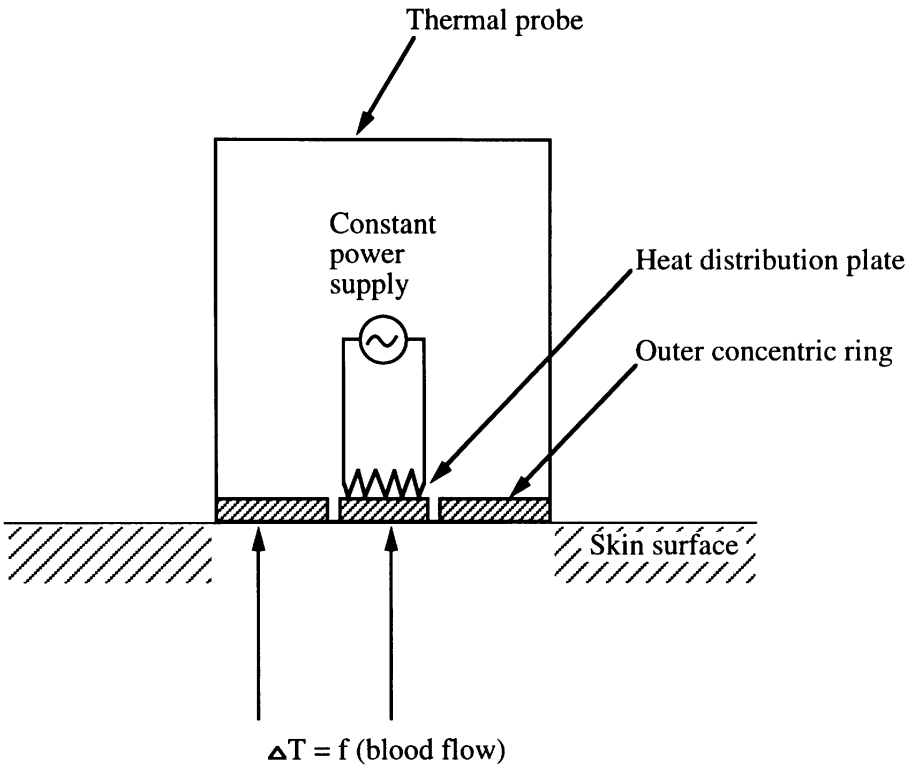

FIGURE 76.7 For thermal convection measurement of blood flow, heat dissipation increases with blood flow.

de Staak et al. [21] developed noninvasive variants by designing probes that can be positioned at the surface of the tissue.

All methods measure the rate of removal of heat from the tissue volume under the probe. A relation exists between the blood flow rate and the rate by which heat dissipates from the tissue volume under study. The sensing unit is usually designed around a central metal disk and a concentric outer ring between which a temperature difference is established. (Figure 76.7). The two rings are thermally and electrically isolated from each other and both are in contact with the tissue. The temperature difference between the two rings is a measure of the blood flow under the probe.

A temperature difference of 2 to 3°C is usually established between the inner disk and the outer annulus. The central disk is heated with an electric current and kept at a constant temperature that only by 1 or 2°C exceeds the resting temperature of the tissue under study. Thermal probes have not been extensively used because of their extreme nonlinear properties and the difficulties in their practical use, i.e., the contact pressure sensitivity. Another difficulty is the highly variable thermal characteristics of the skin.

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