Other Quantitative Techniques

10

Introduction

This chapter examines four quantitative techniques that do not fit easily into the preceding chapters (Table 10.1). One is a quantitative technique with general applicability, and the other three are nuclear medicine studies with unusual quantitative techniques. The body surface area normalization technique is a general method to determine whether an equation that measures a biologic function in absolute terms should be normalized for body surface area (BSA). The Cystogram - Direct Study with Tc-99m-DTPA is performed primarily to detect vesicoureteral reflux during either bladder filling or voiding. However, the study can also be used to measure the post-void residual volume of urine in the bladder. The GLOFIL® study uses an intravenous injection of I-125-iothalamate, a molecule that is cleared from the blood by glomerular filtration, to measure renal clearance in absolute terms. The study involves blood and urine sampling but no imaging. And Cisternogram with In-111-DTPA is performed mainly to evaluate the flow of cerebrospinal fluid (CSF) from the lumbar subarachnoid space to the superior sagittal sinus. However, in patients with suspected CSF rhinorrhea, the study can be modified to help detect and locate the site of a leak and to roughly quantitate the amount of leak.

Body Surface Area Normalization

General

There are several quantitative measurements of the clearance of substances from the blood in laboratory medicine as well as in nuclear medicine that require normalization for body surface area before a single normal range can be used for all patients regardless of size. At the same time, there are other quantitative measurements in which normalization for BSA is inherent in the method and secondary

W.C. Klingensmith III, *The Mathematics and Biology of the Biodistribution of Radiopharmaceuticals-A Clinical Perspective*,
DOI 10.1007/978-3-319-26704-3_10

Table 10.1 Other nuclear medicine studies involving quantitative techniques

Procedure	Radiopharmaceutical	Functional parameter
General		
Body surface area normalization	N/A	Body surface area normalization
Central nervous system		
Cisternography	In-111-DTPA	CSF rhinorrhea
Genitourinary system		
Cystogram – Direct	Tc-99m-DTPA	Post-void residual urine volume
GLOFIL® Study	I-125-iothalamate	Glomerular filtration (clearance)

normalization for BSA is not required. In at least one nuclear medicine study, the Renal Tubular Secretion Study with Tc-99m-MAG3, there has been disagreement in the literature relative to whether the result should be normalized for BSA [1]. The body surface area normalization procedure is a mathematical technique that directly determines whether an equation should be normalized for BSA.

In order to calculate a clearance rate of any substance from the blood, two pieces of information are needed: (1) the amount of test substance transferred from blood into the organ in question during a given period of time and (2) the amount of test substance in the blood or plasma that was available for clearance during the same period of time. The measurement of test substance may be in terms of the concentration of the test substance in the blood, e.g., plasma creatinine on a milligram per milliliter basis, or on the basis of the total dose of radiopharmaceutical that is injected intravenously at the start of the study in millicuries. The amount of cleared test substance goes in the numerator and the amount of available test substance in blood over the relevant time period goes in the denominator. In the case of a clearance measurement with a radiopharmaceutical that is injected in its entirety at the beginning of the study, there is a conversion factor in the numerator with units of "mL".

In general, the technique for determining whether normalization for BSA is needed involves: (1) expanding the numerator and denominator of the clearance equation in question, (2) substituting the term "BSA" for each factor that varies with patient size and "1" for each factor that does not vary with patient size, and (3) simplifying the transformed equation. If the result is "BSA," the measurement varies with BSA and needs to be multiplied by "1.73 m^2/BSA_P" where "BSA_P" is the patient's BSA. If the result is "1," the measurement does not vary with BSA and does not need to be normalized for BSA. And, if the result is "1/BSA," the measurement varies inversely with BSA and needs to be multiplied by "$BSA_P/1.73\ m^2$."

The studies listed in Table 10.2 all include a measurement of clearance in absolute terms. Notice that the list includes the creatinine clearance test, a non nuclear medicine study, and the GLOFIL® test, which does not involve imaging and is not discussed elsewhere in this book. All of these studies measure the clearance rate from blood into an organ or a lesion (in the case of the glucose tumor metabolism with F-18-FDG) and will be analyzed for the need to perform secondary normalization for BSA.

Table 10.2 Studies with absolute quantification and the mechanism for BSA normalization

Procedure	Radiopharmaceutical	Functional parameter	Comment	Blood sampling	Normalization for BSA
Endocrine system					
Thyroid uptake measurement	I-123	Thyroid uptake (clearance)	Organ based	No	Inherent (via blood volume)
Genitourinary system					
Creatinine clearance test (non nuclear medicine study)	Creatinine	Glomerular filtration (clearance)	Organ based	Yes	Secondary (via BSA)
Renal Glomerular Filtration Study	Tc-99m-DTPA	Glomerular filtration (clearance)	Organ based	No	Inherent (via blood volume)
Renal Tubular Excretion Study	Tc-99m-MAG3	Tubular excretion (clearance)	Organ based	No	Inherent (via blood volume)
GLOFIL®	I-125-iothalamate	Glomerular filtration (clearance)	Organ based	Yes	Secondary (via BSA)
Tumor imaging					
Tumor Glucose Metabolism Study	F-18-FDG	Glucose metabolism (clearance)	Gram based	No	Inherent (via body weight)

Table 10.3 Parameters affecting renal clearance of creatinine

Patient size	Kidney size	Renal blood flow	Plasma volume	EE	Creatinine production	Creatinine plsm conc	Creatinine excreted	BSA correction
Average	–	–	–	–	–	–	–	Yes
Small	↓	↓	↓	–	↓	–	↓	Yes
Large	↑	↑	↑	–	↑	–	↑	Yes
						Denominator	Numerator	

– average or unchanged, ↓ decreased; ↑ increased, *EE* extraction efficiency, *plsm conc* plasma concentration

Creatinine Clearance Test

We start with the non nuclear medicine creatinine clearance test. Table 10.3 evaluates the relationship between patient size and the creatinine clearance rate in a conceptual, non-mathematical manner [1]. Three patient sizes are listed: average, small, and large. Notice that the physiologic parameters, kidney size, renal blood flow, blood volume, and creatinine production, all vary with patient size or BSA. On the other hand, the extraction efficiency for glomerular filtration does not vary with

patient size. And, because creatinine production and blood volume both vary directly with patient size, the blood creatinine concentration does not vary with patient size. However, the amount of creatinine excreted will vary directly with patient size because renal blood flow varies directly with patient size and, therefore, the creatinine clearance result will require normalization for BSA. The terms "denominator" and "numerator" at the bottom of Table 10.3 indicate that the parameters "Creatinine plsm conc" and "Creatinine excreted" go in the denominator and numerator of the renal clearance equation, respectively.

Now we will look at the same question, i.e., whether normalization for patient size is needed in the creatinine clearance measurement, from a mathematical point of view. The relevant equation for renal creatinine clearance, Cl (mL/min), before any secondary normalization for BSA, is,

$$\mathrm{Cl}\left(\mathrm{mL/min}\right) = \frac{U\left(\mathrm{mg/min}\right)}{P\left(\mathrm{mg/mL}\right)} \tag{10.1}$$

Here U is the amount of creatinine in a 24 h urine collection on a per minute basis and P is the plasma concentration of creatinine in milligrams per milliliter. The initial step of multiplying the concentration of creatinine in the 24 h urine collection times the urine volume has been omitted.

When the creatinine clearance equation is normalized for BSA, the ratio, 1.73 m^2/BSA_P, is added where 1.73 m^2 is the BSA of a normal-sized person and BSA_P is the BSA of the patient with units of meters squared understood,

$$\mathrm{Cl}\left(\mathrm{mL/min}\right) = \frac{U\left(\mathrm{mg/min}\right)}{B\left(\mathrm{mg/mL}\right)} \times \frac{1.73\ \mathrm{m}^2}{\mathrm{BSA_P}} \tag{10.2}$$

Equation 10.2 indicates that the renal clearance result with the creatinine clearance method is explicitly normalized for BSA.

At this point we return to Eq. 10.1 and expand the numerator and denominator. First, we expand the numerator that represents the amount of test substance cleared in a certain amount of time into the physiologic factors that determine the amount of test substance that is cleared. These factors, as discussed in detail in Chap. 4, Evaluation of Clearance, are blood flow to the kidneys, F (mL/min-kidneys); the extraction efficiency for the test substance in question, which will depend primarily on the extraction mechanism, EE (no units); and the concentration of the test substance in plasma as a function of time during the uptake period: $\int_0^T P(\mathrm{t})\,\mathrm{d}t\left(\mathrm{mCi-min/mL}\right)$. Here T is the time at the end of the urine collection, 24 h. The final equation for creatinine uptake in the numerator is,

$$U\left(\mathrm{mg/min}\right) = F\left(\mathrm{mL/min}\right) \times \mathrm{EE} \times \int_0^T P\left(t\right)\mathrm{d}t\left(\mathrm{mg-min/mL}\right) / T\left(\mathrm{min}\right) \tag{10.3}$$

Substituting the right-hand side of Eq. 10.3 into Eq. 10.1 and expanding the factor P in both the numerator and denominator gives,

$$\mathrm{Cl}(\mathrm{mL/min}) = \frac{F(\mathrm{mL/min}) \times \mathrm{EE} \times \int_0^T [\mathrm{TPCr/TPV}](t)\,\mathrm{d}t(\mathrm{min}) / T(\mathrm{mg-min/mL})}{\mathrm{TPCr}(\mathrm{mg}) / \mathrm{TPV}(\mathrm{mL})} \tag{10.4}$$

where TPCr is total plasma creatinine and TPV is total plasma volume.

Now we can substitute either BSA or 1 for each physiologic factor depending on whether the factor varies with patient size. This gives,

$$\mathrm{Cl}(\mathrm{mL/min}) \sim \frac{\mathrm{BSA} \times 1 \times [\mathrm{BSA/BSA}] \times 1/1}{\mathrm{BSA/BSA}} \tag{10.5}$$

which reduces to,

$$\mathrm{Cl}(\mathrm{mL/min}) \sim \mathrm{BSA} \tag{10.6}$$

indicating that renal clearance, as measured by the creatinine clearance method, varies with patient size, and therefore, the result requires normalization for BSA. Note that when the normalization factor shown in Eq. 10.2 is added to Eq. 10.6, the BSA in Eqs. 10.2 and 10.6 cancel so that the creatinine clearance result no longer varies with BSA, i.e., it has been normalized for BSA. Also, note that in the equations in this chapter, the symbol '~' is used to mean "varies with."

Organ-Based Clearance Studies with Radiopharmaceutical Imaging

Now we apply a similar analysis to those nuclear medicine studies that involve administration of a radiopharmaceutical followed by imaging that depicts the clearance of radiopharmaceutical from blood into an organ in absolute terms [1]. These studies are the Renal Tubular Secretion Study with Tc-99m-MAG3, the Renal Glomerular Filtration Study with Tc-99m-DTPA, and the Thyroid Uptake Study with I-123. Both the conceptual and mathematical analyses are the same for all three studies. These three studies are organ based.

Table 10.4 evaluates the relationship between patient size and the organ clearance rate in a conceptual, non-mathematical manner for radiopharmaceutical methods [2]. Again, three patient sizes are listed, average, small, and large, and again, the physiologic parameters organ size, organ blood flow, and blood volume all vary with patient size or BSA. Because tracer dose can be assumed to be the same for all patient sizes and blood volume varies directly with patient size, the blood tracer

Table 10.4 Parameters affecting clearance of radiopharmaceuticals into organs

Patient size	Organ size	Organ blood flow	Plasma volume	EE	Tracer dose	Tracer plsm conc	Tracer uptake	BSA correction
Average	–	–	–	–	–	–	–	No
Small	↓	↓	↓	–	–	↑	–	No
Large	↑	↑	↑	–	–	↓	–	No
					Denominator		Numerator	

– average or unchanged, ↓ decreased, ↑ increased, *EE* extraction efficiency, *plsm conc* plasma concentration

concentration will vary inversely with patient size. The extraction efficiency for all three studies will not vary with patient size. The end result is that the amount of tracer cleared will not vary with patient size because, while the organ blood flow varies directly with patient size, the tracer concentration in the blood varies inversely with patient size. Thus, the result does not require correction for BSA. The terms "denominator" and "numerator" at the bottom of Table 10.4 indicate that the parameters "tracer dose" and "tracer uptake" go in the denominator and numerator of the renal clearance equation, respectively.

Now we will look at the same question, i.e., whether correction for patient size is needed in organ-based tracer clearance measurements, from a mathematical point of view. The relevant equation for organ clearance, Cl (mL/min), is,

$$\mathrm{Cl}\left(\mathrm{mL/min}\right) = \frac{F\left(\mathrm{mL/min}\right) \times \mathrm{EE} \times \int_0^T \left[D/\mathrm{TPV}\right](t)\,\mathrm{d}t \;\left(\mathrm{min-cpm/mL}\right)}{D\left(\mathrm{cpm}\right)} \tag{10.7}$$

where F is blood flow, EE is extraction efficiency, D is total plasma tracer, TPV is total plasma volume, and T is time from injection to the end of acquisition of the clearance image. The conversion factor in the numerator with units of mL/min has been left out. The conversion factor converts percent uptake on the right-hand side of the equation to clearance on the left and is a constant.

Now we substitute either BSA or 1 for each physiologic factor depending on whether the factor varies with patient size,

$$\mathrm{Cl}\left(\mathrm{mL/min}\right) \sim \frac{\mathrm{BSA} \times 1 \times \left[1/\mathrm{BSA}\right] \times 1}{1} \tag{10.8}$$

Table 10.5 Parameters affecting clearance of glucose into tumor as standard uptake value (SUV)

Patient size	Tumor size per gram	Tumor blood flow per gram	Blood volume	EE	Tracer dose per gram	Tracer bld conc	Tumor uptake per gram	BSA correction
Average	–	–	–	–	–	–	–	No
Small	–	–	↓	–	↑	↑	↑	No
Large	–	–	↑	–	↓	↓	↓	No
					Denominator		Numerator	

– average or unchanged, ↓ decreased, ↑ increased, *EE* extraction efficiency, *bld conc* blood concentration

which reduces to,

$$\mathrm{Cl}\left(\mathrm{mL}/\mathrm{min}\right) \sim 1 \tag{10.9}$$

indicating that the result does not need to be normalized for BSA.

Gram of Tissue-Based Studies with Radiopharmaceutical Imaging

Now we apply the same analysis to clearance of FDG into tumor in the Tumor Glucose Metabolism Study [2–4]. The equation for the SUV is,

$$\mathrm{SUV} = \frac{\mathrm{FDG\,in\,tissue}\left(\mathrm{mCi}/\mathrm{mL}\right)\left(\mathrm{mL}/\mathrm{gm}\right)}{\mathrm{Dose}\left(\mathrm{mCi}\right)/\mathrm{Body\,weight}\left(\mathrm{gm}\right)} \tag{10.10}$$

Here, unlike the three organ-based clearance studies above, the tumor uptake (clearance) is on a per volume basis and the tracer dose is on a per gram basis. Note that in the numerator it is assumed that a gram corresponds to a milliliter although this is not always the case.

Table 10.5 evaluates the relationship between patient size and the tumor clearance in a conceptual, non-mathematical manner. Again, three patient sizes are listed: average, small, and large. Notice that, unlike the physiologic parameters in Tables 10.3 and 10.4, the parameters tumor size per gram and tumor blood flow per gram do not vary with patient size or BSA. The extraction efficiency will not vary with patient size. Because the tracer dose can be assumed to be the same for all patient sizes and blood volume varies directly with patient size, the blood tracer concentration will vary inversely with patient size. In addition, the tracer dose per gram and tumor uptake per gram vary inversely with patient size. Because the tracer

dose per gram is in the denominator and the tumor uptake per gram is in the numerator, the inverse effect of size cancels and the SUV will not vary with patient size. Thus, the result does not require normalization for BSA.

Now we will look at the same question, i.e., whether normalization for patient size is needed in the measurement of the SUV in the Tumor Glucose Metabolism Study, from a mathematical point of view. The relevant equation for SUV (unitless) after expansion is,

$$\mathrm{SUV} = \frac{F\left(\mathrm{mL/min-gm}\right)\times \mathrm{EE}\times P_{\mathrm{Nl}}/P_{\mathrm{Act}}\times\int_0^T\left[D/\mathrm{TBV}\right](t)\,\mathrm{d}t\ \left(\mathrm{mCi-min/mL}\right)}{D\left(\mathrm{mCi}\right)/\mathrm{Body\,weight}\left(\mathrm{gm}\right)} \tag{10.11}$$

where $P_{\mathrm{Nl}}/P_{\mathrm{Act}}$ is the ratio of the normal concentration of glucose in the blood to the actual concentration of glucose in the blood. The ratio of normal to injected glucose is included here because the extraction mechanism for glucose transport into the cell is saturable. The other variables are defined above.

Now we can substitute either BSA or a 1 for each physiologic factor depending on whether the factor varies with patient size,

$$\mathrm{SUV} \sim \frac{1\times 1\times 1\times\left[1/\mathrm{BSA}\right]\times 1}{1/\mathrm{BSA}} \tag{10.12}$$

which reduces to,

$$\mathrm{SUV} \sim 1 \tag{10.13}$$

indicating that the result does not need to be normalized for BSA. Effectively, the *Body weight* factor normalizes the equation for body size. Otherwise, the result would have to be normalized by 1/BSA.

GLOFIL® Study

The GLOFIL® study is a non-imaging study that is performed with an intravenous injection of I-125-iothalamate. The ligand, iothalamate, is a CT contrast material [5]. I-125-iothalamate is cleared in the kidneys by glomerular filtration. Beginning 45 min after injection of the radiopharmaceutical, the patient empties his/her bladder and blood sample #1 is obtained. Forty-five minutes later, the patient again empties his/her bladder as urine sample #1 and blood sample #2 is obtained. After another 45 min, the patient again empties his/her bladder as urine sample #2 and blood sample #3 is obtained (Fig. 10.1).

The radioactivity in the urine and blood samples is measured on a per milliliter basis and the two plasma values on either side of the two urine collections are averaged. If the blood level of tracer decreased in a linear fashion, the clearance rate of tracer obtained by dividing the tracer in the each urine collection by the mean of the beginning and ending blood concentration of tracer would be accurate. However, since the decrease in blood tracer over time is exponential, the result will underestimate the clearance rate by a small amount (Fig. 10.1).

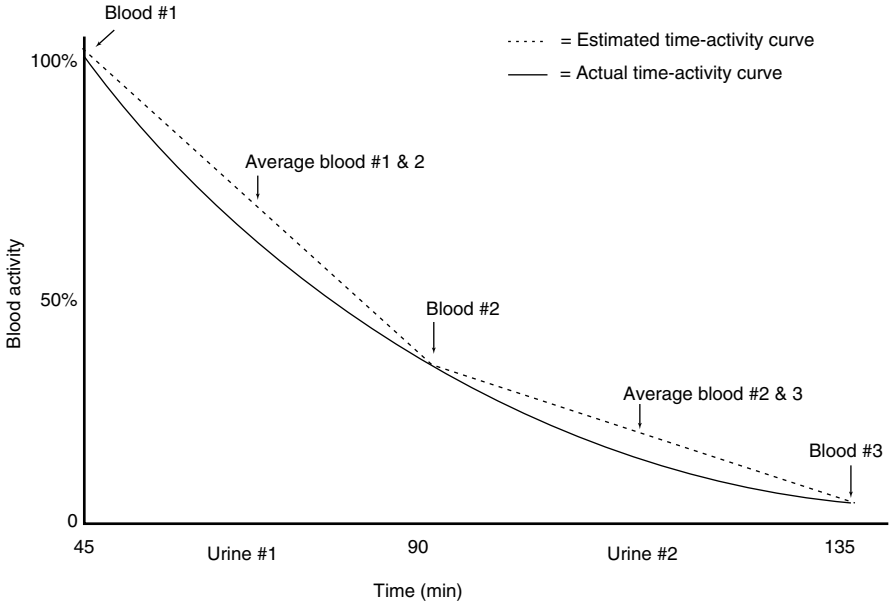

Fig. 10.1 Graph of "blood activity" vs. "time." Note that time on the *X*-axis starts at 45 min. There are three blood collections at 45, 90, and 135 min and two urine collections at 90 and 135 min. The first and second blood collections and the second and third blood collections are averaged to match the urine collections

Table 10.6 Parameters affecting renal clearance with GLOFIL® method

Patient size	Renal size	Renal blood flow	Blood volume	EE	Tracer dose	Tracer bld conc	Tracer excreted	BSA correction
Average	–	–	–	–	–	–	–	Yes
Small	↓	↓	↓	–	–	↑	–	Yes
Large	↑	↑	↑	–	–	↓	–	Yes
						Denominator	Numerator	

– average or unchanged, ↓ decreased, ↑ increased, *EE* extraction efficiency, *bld conc* blood concentration

Table 10.6 analyzes the effect of patient size on various physiologic and tracer parameters. Again, three patient sizes are listed: average, small, and large. Notice that the physiologic parameters renal size, renal blood flow, and blood volume all vary with patient size or BSA, while the extraction efficiency will not vary with patient size. Because tracer dose can be assumed to be the same for all patient sizes but blood volume varies directly with patient size, the blood tracer concentration will vary inversely with patient size. At the same time, the amount of tracer cleared and excreted will not vary with patient size because the direct effect of patient size on renal blood flow is offset by the inverse effect of patient size on blood tracer concentration. Since the amount of tracer excreted in the urine is measured and goes

in the numerator and the concentration of tracer in the blood is measured and goes in the denominator, the glomerular filtration clearance rate will need to be normalized for patient size, i.e., BSA.

Now we will look at the same question, i.e., whether correction for patient size is needed in the GLOFIL® measurement of renal clearance, from a mathematical point of view. The equation for renal clearance by glomerular filtration prior to any normalization for BSA and using the symbols from the Product Insert is,

$$C\left(\text{mL}/\text{min}\right)=\frac{U\left(\text{cpm}/\text{mL}\right)\times V\left(\text{mL}/\text{min}\right)}{P\left(\text{mean cpm}/\text{mL}\right)} \tag{10.14}$$

where C is renal clearance rate by glomerular filtration in milliliters per minute, U is urine radioactivity in counts per minute per milliliter, V is urine flow rate in milliliters per minute, and P is mean plasma radioactivity in counts per minute per milliliter.

We then expand Eq. 10.14 and revert to the symbols used throughout this book to give,

$$\text{Cl}\left(\text{mL}/\text{min}\right)=\frac{F\left(\text{mL}/\text{min}\right)\times \text{EE}\times \int_{45}^{135}\left[D/\text{TBV}\right]\text{d}t\left(\text{min}\right)/T\left(\text{min}-\text{cpm}/\text{mL}\right)}{D\left(\text{cpm}\right)/\text{TBV}\left(\text{mL}\right)} \tag{10.15}$$

where "45" and "135" are the times (in minutes) of the start and end of the study relative to the time of injection of the radiopharmaceutical.

Now we can substitute either BSA or 1 for each physiologic factor depending on whether the factor varies with patient size, to give,

$$\text{Cl}\left(\text{mL}/\text{min}\right)\sim \frac{\text{BSA}\times 1\times\left[1/\text{BSA}\right]\times 1/1}{1/\text{BSA}} \tag{10.16}$$

which reduces to,

$$\text{Cl}\left(\text{mL}/\text{min}\right)\sim \text{BSA} \tag{10.17}$$

indicating that the result must be normalized for BSA. The final GLOFIL® equation is,

$$C\left(\text{mL}/\text{min}\right)=\frac{U\left(\text{cpm}/\text{mL}\right)V\left(\text{mL}/\text{min}\right)}{P\left(\text{mean cpm}/\text{mL}\right)}\times\frac{1.73\ \text{m}^2}{\text{BSA}} \tag{10.18}$$

In summary, with proper manipulation an equation that measures a physiologic or molecular biologic parameter can be made to indicate whether it must be normalized for BSA or not.

Cystogram - Direct

The Direct Cystogram with Tc-99m-DTPA is performed primarily in children to detect vesicoureteral reflux. However, the images and voided urine volume can be used to noninvasively determine the post-void residual volume of urine in the bladder [6]. Figure 10.2 shows a cross-sectional diagram of a patient at the level of the bladder pre void and post void with some post-void residual urine in the bladder.

ROIs are placed around the bladder in the two diagrams (broken lines) and the counts per minute are measured. The volume of voided urine is also measured. Then the formula for determining the post-void residual urine volume is,

$$\mathrm{RBV}(\mathrm{mL}) = \frac{\mathrm{RBA}(\mathrm{cpm}) \times \mathrm{VU}(\mathrm{mL})}{\mathrm{FBA}(\mathrm{cpm}) - \mathrm{RBA}(\mathrm{cpm})} \tag{10.19}$$

where RBV is residual bladder volume in milliliters, RBA is residual bladder activity in counts per minute, VU is voided urine in milliliters, and FBA is full bladder activity in counts per minute.

Equation 10.19 can be rearranged to prove that RBV (mL) represents the residual bladder volume,

$$\frac{\mathrm{RBV}(\mathrm{mL})}{\mathrm{RBA}(\mathrm{cpm})} = \frac{\mathrm{VU}(\mathrm{mL})}{\mathrm{FBA}(\mathrm{cpm}) - \mathrm{RBA}(\mathrm{cpm})} = \frac{\mathrm{VU}(\mathrm{mL})}{\mathrm{VUA}(\mathrm{cpm})} \tag{10.20}$$

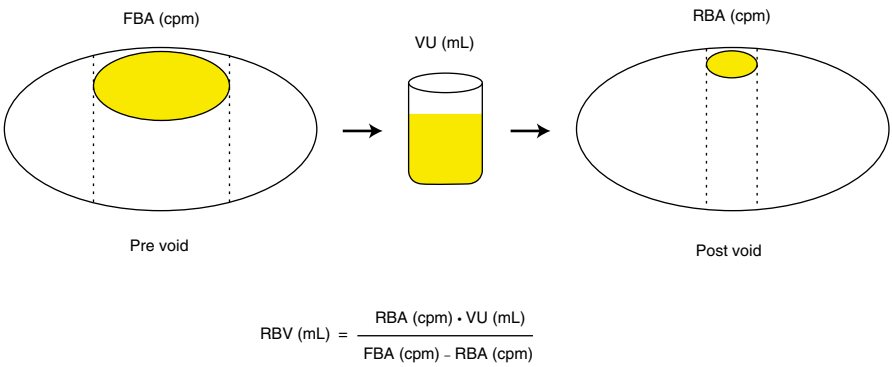

Fig. 10.2 Diagrams of the same pelvic cross section through the bladder pre and post void. The broken lines depict ROIs over the bladder. The equation for calculating the residual bladder volume is shown

Equation 10.20 demonstrates that the ratio of residual bladder volume, RBV (mL), to residual bladder activity, RBA (cpm), on the left side of the equation equals the ratio of voided urine volume, VU (mL), to voided urine activity, VUA (cpm), on the right side of the equation. Therefore, urine activity in counts per minute directly reflects urine volume in milliliters once a change in bladder activity is calibrated to a known change in urine volume [6]. VUA is voided urine activity, but it is unmeasured because the photon attenuation in a beaker would not match the photon attenuation of urine in the bladder.

Cisternography with Nasal Pledgets

When the Cisternography with In-111-DTPA study is done for the purpose of diagnosing CSF rhinorrhea and identifying its location, nasal pledgets of a standard size are placed in the anterior and posterior portions of both nasal cavities 2 h after the intrathecal injection of In-111-DTPA and removed 4 h later [7]. In addition, blood samples are drawn at the same times. The pledget and plasma specimens are counted in a gamma well counter, and the results are expressed as the ratio of the amounts of activity in the pledgets, i.e., nasal cavities, relative to the amount of activity in plasma,

$$\mathrm{NPR} = \frac{P_{\mathrm{Act}}\left(\mathrm{cpm}/0.5\,\mathrm{mL}\right)}{B_{\mathrm{Act}}\left(\mathrm{cpm}/0.5\,\mathrm{mL}\right)} \tag{10.21}$$

Here, NPR is the nasal pledget to plasma ratio, P_{Act} is pledget activity in counts per minute per 0.5 mL (the volume of fluid that a pledget is expected to absorb), and B_{Act} is activity in counts per minute per 0.5 ml of plasma [7].

This measurement represents a quasi-absolute measurement. The amount of activity in the pledgets (reflecting the degree of leakage of labeled CSF from the subarachnoid space through a break in the dura and skull base into the nasal cavities) goes in the numerator, and the amount of activity in the plasma (serving as a proxy for the amount of In-111-DTPA that was administered intrathecally) goes in the denominator. There is no need to correct for background activity or attenuation.

However, there is a significant weakness in the approach of the cisternogram to measuring the amount of In-111-DTPA that leaks into the nasal cavity. In-111-DTPA primarily reaches the blood as CSF is absorbed into the superior sagittal sinus by the arachnoid villa. But, it takes nearly 24 h for the tracer to pass from the lumbar region of the subarachnoid space to the convexity of the brain. Yet the nasal pledgets are removed from the nasal cavity at 6 h after injection of the tracer. The In-111-DTPA that is in the blood at the time of the 2 and 6 h blood samples probably leaks across the subarachnoid membrane and dura at the lumbar injection site and then passes with lymph flow into the vascular space. Other pathways are also possible.

The clinical application of to Cisternography is discussed more fully in Chap. 13: Central Nervous System.

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