Kinetic Analyses of Parathyroid Hormone Clearance as Measured by Three Rapid Immunoassays during Parathyroidectomy

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Background: Rapid intraoperative parathyroid hormone (PTH) measurements are an important prerequisite for minimally invasive parathyroidectomy, serving as a feasible marker for “cure” because of the short half-life of PTH. Because automated analysis may facilitate monitoring, two automated PTH assays were compared with an established manual method.

Methods: We collected 109 plasma samples during minimally invasive surgery on 20 patients with primary hyperparathyroidism and single-gland disease. PTH was analyzed manually with a test from Nichols and by two automated assays from Diagnostic Product Corporation (DPC) and Roche, respectively. PTH half-life and residual concentrations were calculated by two kinetic models.

Results: Despite good overall correlations between methods [DPC = 1.07(Nichols) – 12 ng/L; r = 0.95, Sd = 26 ng/L and Roche = 1.16(Nichols) – 2.82 ng/L; r = 0.98; Sd = 16 ng/L], marked interindividual differences were observed. The iterative kinetic model failed with a nonuniform PTH decrease, but the interpolative model produced valid results. The mean (SD) half-life of 3.7 ± 1.4 min with DPC differed significantly (P <0.05) from the 4.3 ± 1.6 min with Roche (Nichols, 4.0 ± 1.6 min). DPC produced significantly lower mean residual PTH (15 ng/L) vs Roche (27 ng/L); Nichols results were between them (20 ng/L). However, these differences were clinically irrelevant.

Conclusions: Automated methods are as suitable as the manual test. The preoperative baseline PTH is necessary but is insufficient for kinetic calculations.

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Surgical treatment of patients suffering from biochemically confirmed primary hyperparathyroidism (pHPT)3 is undergoing an evolution. The traditional surgical approach visualizing all four parathyroids and resecting the apparently enlarged gland(s) has been increasingly replaced by minimally invasive (unilateral) surgical procedures aided by preoperative imaging and intraoperative rapid parathyroid hormone (PTH) measurements (1–8). In most cases, the improved imaging techniques enable exact preoperative localization of the parathyroid adenoma (9). PTH monitoring during the surgical procedure can confirm the removal of all hyperfunctioning parathyroid tissue as the half-life of intact (1–84) PTH is short. An insufficient decrease in PTH indicates persisting pHPT, leading to more extended (bilateral) exploration within the same session. Although PTH monitoring ignores possible changes in the physiologic state of the patient during surgery (e.g., changes of clearing rate) and is deemed invalid if the volume is expanded by intraoperative infusions, it helps to reduce the frequency of repeat surgery.

Measurement of PTH has also undergone evolution. The early generation of PTH RIAs was restricted to N-terminal, midregion, or C-terminal fragments, all of which circulate in high concentrations as they are cleared slowly (10, 11). By use of two monoclonal antibodies specific for the N- and C-terminal regions of the hormone (12), rapid measurement of intact (1–84) PTH became feasible. The sensitivity of tests was further improved by replacement of radiolabels with chemiluminescent groups. Special assay formats allow rapid detection within 15 min, a time-span suitable for intraoperative PTH monitoring (2). To test whether automated analysis

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3 Nonstandard abbreviations: pHPT, primary hyperparathyroidism; PTH, parathyroid hormone; and DPC, Diagnostic Product Corporation.
by a new generation of assays provides reliable results, we compared two recently developed methods running on immunoassay analyzers with an established manual assay for quick PTH.

Commonly, a 50% decrease versus baseline PTH 5–10 min after resection of the suspected parathyroid adenoma indicates “cure” (1). However, the definition of this “baseline” seems vague, especially as plasma PTH is markedly influenced by surgical manipulations during preparation of the affected gland(s). In addition, the recommendation does not account for interindividual variability of PTH half-life and residual concentration (13). We evaluated these crucial factors by two kinetic models and addressed several questions: (a) Which model fits better to the PTH results and which starting concentration is relevant for kinetic calculations (the preoperative baseline or the PTH concentration just at adenectomy)? (b) Do the assays produce comparable kinetic results and is there an advantage in using automated PTH analyses? (c) Can intraoperative kinetic calculations support the assessment of PTH patterns?

Patients and Methods

Patients
To date, minimally invasive parathyroidectomy has been performed at our institution (9) in >170 patients suffering from pHPT. Patients gave informed consent for surgery and blood collection via an extra catheter. All operations were performed by the same surgeon (B.N.). We report here on 20 consecutive patients (18 females and 2 males; mean age, 57.8 ± 12.1 years) with single-gland disease. Renal failure was excluded in all these patients. Adenomas were localized preoperatively by high-resolution ultrasound and by 99mTc-sestamibi scans with single photon emission computed tomography. Blood was collected before skin incision (preoperative baseline concentration), at the time of adenoma resection, and thereafter at intervals of 5 min (0, 5, 10, and 15 min). The surgeon asked for additional blood samples from some patients (e.g., in case of prolonged adenoma preparation or a slow decrease in PTH); the exact time points of these samples were documented. Blood specimens were centrifuged for 1 min in Eppendorf cups and subsequently analyzed.

Success of surgical intervention was judged by an intraoperative PTH decrease (at least 50% within 10 min after adenectomy) related to the preoperative baseline PTH. In case of atypical PTH increase until adenectomy, a later sample was collected for confirmation. Parathyroid tissue was examined histologically. At 1 year after operation, calcium was normal in all patients.

Analytical Methods and Organization

Two chemiluminescence immunoassays [QuiCk-IntraOperative^TM intact PTH (Nichols Laboratories) and Turbo-PTH-intact (Diagnostic Products Corporation; DPC)] and one electrochemiluminescence method (intact-PTH; Roche-Diagnostics) were used for rapid PTH measurements. All assays had been evaluated previously (1–8, 14–16) and are approved by the US Food and Drug Administration. The manual assay by Nichols was carried out with the “QuiCk-Pack” system from Nichols Laboratories. If the CV of duplicates exceeded 10%, the sample was reanalyzed. The DPC assay was performed on the Immuno-1 automated analyzer (DPC). The Roche intact-PTH test was performed on an Elecsys-1010 immunoassay analyzer (Roche Diagnostics) with its “Stat-function”. Single determinations were sufficient with automated methods, because CVs of duplicates were <4%. Instruments maintenance and test calibration were performed in the main laboratory.

The analytical instruments and other laboratory tools were transported on trolleys to the operating theater, where control samples were reanalyzed. Ten patients were monitored intraoperatively with the Nichols test and another 10 with the Roche test. Direct contact was always possible between surgical and analytical teams because samples were processed in a preparation room adjacent to the operating theater. However, there was too little space for two trolleys; thus, immediate comparative analyses with the other tests were performed in the main laboratory on sample aliquots transported in an ice bath. Although the DPC analyzer could have been transported on a large trolley, for organizational reasons the comparative data on the DPC assay were collected retrospectively from samples stored at −80 °C. Marked influence of one freezing/thawing had been excluded in a pre-experiment.

Assay precision was determined by use of control samples supplied by the respective companies. Day-to-day CVs (n = 12) were 17% (37 ng/L) and 9% (251 ng/L) for the Nichols, 11% (84 ng/L) for the DPC, and 7% (at 54 and 169 ng/L) for the Roche EL1010, respectively. Intraassay CVs (n = 6) were 9% and 7% (Nichols), 6% (DPC), and 4% and 3% (Roche) at the control sample concentrations indicated above.

Method Comparisons and Statistics

Method comparisons (17) were calculated from 109 samples, and individual comparisons for each patient were calculated as well (5–10 samples per patient). Significance of differences (P <0.05) was evaluated by ANOVA and the Tukey–Kramer post-test.

Kinetic Analyses

Intraoperative PTH half-life and the residual concentrations were calculated by two kinetic models by use of Microsoft Excel on a personal computer. Model A was recently published by Libutti et al. (13) and describes relief of the total suppressed PTH secretion from healthy glands after adenectomy. In this model (Fig. 1, top), the exponential decay of PTH from the adenoma (concentration \( c_0 \) is the measured concentration at time \( t \) and \( \Delta c_0 \), where \( c_0 = c_i + \Delta c_0 \), where \( c_0 \) is the concentration at time \( t = 0 \), and \( k \) is the rate constant of decay) is superimposed by a time-dependent additive concentration \( c_m = c_i + \Delta c_i \).
is the additive concentration at time t). This additive concentration stems from the healthy glands, which recover PTH secretion, and is a function of a constant residual PTH concentration R, which is calculated according to Libutti et al. (13) (Eqs. 3 and 4) by:

$$ R = \frac{\Delta c_t (2^{kt/\ln2})}{2^{kt/\ln2} - 1} $$

thus:

$$ \Delta c_t = R - Re^{-kt} $$

Because \( \Delta c_t = c_m - c_0e^{-kt} \), the equation may be expressed as:

$$ R = \frac{c_m e^{kt} - c_0}{e^{kt} - 1} \quad (1) $$

and solved for k:

$$ k = \frac{\ln((c_0 - R)/(c_m - R))}{t} \quad (2) $$

For iterative calculations, Libutti et al. (13) used a preoperative baseline PTH concentration (instead of a true \( c_0 \)); \( c_1 \) and \( c_2 \) were the concentrations 5 and 10 min after adenectomy. Briefly, \( k \) (Eq. 2) was approximated in a first iterative step from \( c_0 \) and \( c_1 \) by assuming \( R = c_2 \). This estimated k value and \( c_2 \) were used to calculate a new \( R \) (Eq. 1), which made calculation of a better fitting k value possible, and so forth. After reaching convergence, the half-life was \( t_{1/2} = \ln2/k \). We performed additional calculations by choosing \( c_0 \) at the time of adenectomy as well as for \( c_3 \) at 15 min.

We developed a second model, basing it on the assumption that the healthy glands were not totally suppressed and secreted constant concentrations of PTH (\( \rho \)) during surgery, adding to the exponential decay of PTH from the removed adenoma (model B; Fig. 1, bottom). Because an exponential decay follows a constant percentage of decrease per identical time intervals (\( i \); e.g., 5 min), the measured concentration \( c_m \) has to be corrected for \( \rho \):

$$ \frac{c_{m, i+1} - \rho}{c_{m, i} - \rho} = a = \text{constant} \quad (3) $$

We set up a matrix (Eq. 4) for calculating the intercept (b) and the slope (a) of a linear regression line: \( y = ax + b \).

$$ x = c_{m, i} \quad y = c_{m, i+1} \quad c_{m0} \quad c_{m1} \quad c_{m1} \quad c_{m2} \quad c_{m2} \quad c_{m3} \quad (4) $$

where \( c_{m0} \) is the PTH concentration at adenectomy.

Combining Eqs. 3 and 4 yields \( \rho = (ax - y)/(a - 1) \). Because \( a = (y - b)/x \), the residual concentration \( \rho \) was calculated (Eq. 5) from the slope and the intercept of the regression line (Fig. 1, inset for model B)

$$ \rho = \frac{-b}{(a - 1)} \quad (5) $$

All measured PTH concentrations were corrected for the residual PTH concentration, followed by an exponential regression analysis: \( \ln(c_m - \rho) = a't + b' \). The decay constant was \( k = -a' \), and the approximated PTH concentration at adenectomy was \( c_{0, \text{app}} = e^{b'} \).

**Results**

The performance and costs of the Nichols, DPC, and Roche tests for rapid PTH differed. The turnaround time from starting the analysis until print-out of results was 16 min for the DPC, 14 min for the Nichols, and 10 min for the Roche assay. Approximately 4 min had to be added to all methods for sample collection, transport to the adjacent room, and centrifugation when the assay was performed at the site of surgery. Although each assay may be performed by a single person, the Nichols manual method
was carried out by two technicians because there was a need for exact time-shifted manipulations. All analytical systems were leased. The costs of reagents per test for the DPC and Roche were 12% and 4%, respectively, of the Nichols test costs. Depending on contracts with the companies, costs may be different for other hospitals. Recently, a detailed cost analysis was presented that included working time and auxiliary costs (18).

Correlation analyses for PTH from 109 samples yielded the following equations: DPC \( /\text{H11005}1.07(\text{Nichols}) = 12 \text{ng/L} \) \( r = 0.95; \sigma_{\text{H11005}} = 26 \text{ng/L} \) and Roche \( /\text{H11005}1.16(\text{Nichols}) = 2.8 \text{ng/L} \) \( r = 0.98; \sigma_{\text{H11005}} = 16 \text{ng/L} \). Deviations between the assays became more obvious when comparability was tested for each patient (Fig. 2). The slopes of the individual regression lines were between 0.56 and 1.67, and their intercepts were between 98 and 17 ng/L (Nichols vs DPC, \( r = 0.92–1.0; \sigma_{\text{H11005}} = 1.8–43 \text{ng/L} \)). Comparisons between Nichols and Roche analyses produced individual slopes from 0.60 to 1.32 and intercepts from 59 to 27 ng/L (\( r = 0.96–1.0; \sigma_{\text{H11005}} = 1.2–20 \text{ng/L} \)).

We next investigated how these discrepancies influenced the calculation of PTH elimination kinetics. Table 1 summarizes the kinetic results obtained from models A and B for the three assays. Model A was applied to data from the preoperative baseline and 5 and 10 min, as suggested by Libutti et al. (13). Use of the PTH at adenectomy instead of the preoperative baseline led to lower residual concentrations (significant for DPC and Roche) and significantly longer half-lives with all assays (mean, 1.8 vs 3.7 min). However, model A calculations led to nonsensical results for 11 patients because of unreasonably high negative residual PTH concentrations and prolonged half-lives. Model B (PTH at adenectomy and 5, 10

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**Table 1. Residual PTH and PTH half-lives calculated by different kinetic models (n = 9 patients).**

<table>
<thead>
<tr>
<th>Residual PTH, ng/L</th>
<th><strong>Time points</strong></th>
<th><strong>Nichols</strong></th>
<th><strong>DPC</strong></th>
<th><strong>Roche</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model A</strong></td>
<td>Baseline,(^a) 5, 10</td>
<td>15 ± 22</td>
<td>18 ± 12(^c)</td>
<td>28 ± 21(^c)</td>
</tr>
<tr>
<td></td>
<td>0, 5, 10</td>
<td>4 ± 4</td>
<td>12 ± 10</td>
<td>11 ± 18</td>
</tr>
<tr>
<td></td>
<td>0, 5, 15</td>
<td>7 ± 12</td>
<td>12 ± 9</td>
<td>22 ± 16</td>
</tr>
<tr>
<td></td>
<td>0, 10, 15</td>
<td>9 ± 17</td>
<td>12 ± 9</td>
<td>23 ± 16</td>
</tr>
<tr>
<td><strong>Model B</strong></td>
<td>0, 5, 10, 15</td>
<td>7 ± 12</td>
<td>12 ± 9</td>
<td>22 ± 16</td>
</tr>
<tr>
<td><strong>PTH half-life, min</strong></td>
<td><strong>Model A</strong></td>
<td>Baseline,(^a) 5, 10</td>
<td>1.7 ± 0.6(^c)</td>
<td>1.7 ± 0.7(^c)</td>
</tr>
<tr>
<td></td>
<td>0, 5, 10</td>
<td>3.6 ± 1.6</td>
<td>3.4 ± 1.3</td>
<td>3.8 ± 1.3</td>
</tr>
<tr>
<td></td>
<td>0, 5, 15</td>
<td>3.6 ± 1.2</td>
<td>3.5 ± 1.2</td>
<td>3.6 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>0, 10, 15</td>
<td>3.7 ± 1.2</td>
<td>3.7 ± 1.3</td>
<td>3.5 ± 0.8</td>
</tr>
<tr>
<td><strong>Model B</strong></td>
<td>0, 5, 10, 15</td>
<td>3.5 ± 1.1</td>
<td>3.3 ± 1.4</td>
<td>3.7 ± 0.9</td>
</tr>
</tbody>
</table>

\(^a\) Model A yielded overall valid kinetic results for only nine patients. Incongruous results were observed as follows: for the (baseline, 5, 10) data set, six each with the Nichols and Roche assays and three with the DPC assay; for the (0, 5, 10) data set, three with the Nichols and one each with the DPC and Roche assays; for the (0, 5, 15) data set, one with the Nichols assay; for the (0, 10, 15) data set, two with the DPC assay. Data sets from the Nichols, DPC, and Roche assays produced invalid results 10, 6, and 7 times, respectively.

\(^b\) Preoperative baseline PTH (before skin incision).

\(^c\) Significantly (P < 0.05) different from other calculations.

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Fig. 2. PTH method comparisons: Nichols vs DPC and Nichols vs Roche.

The individual regression lines from 20 patients were constructed from 5–10 data pairs per patient; all results were within the dynamic range of the assays.
and 15 min) produced meaningful results for all 20 patients and assays. Lower residual PTH values were produced by the DPC (mean, 15 ng/L; range, 1–46 ng/L) and Nichols (mean, 20 ng/L; range, 0–79 ng/L) assays than by the Roche assay (mean, 27 ng/L; range, 0–89 ng/L). The mean half-life was 3.7 ± 1.4 min (range, 1.8–6.0 min) with the DPC, 4.0 ± 1.6 min (range, 1.8–7.7 min) for the Nichols, and 4.3 ± 1.6 min (range, 2.4–8.1 min) for the Roche assay. Differences in residual PTH and half-lives were significant only between the DPC and Roche assays.

Considering whether these differences in kinetic results are clinically relevant, we first inspected the intraoperative PTH patterns. Shown in Fig. 3 are the results when we used the Nichols PTH assay as an example. The time intervals between starting anesthesia and adenectomy ranged from 20 to 77 min, and the average preparation time of the adenoma was 38 min. In 14 of 20 patients, PTH concentrations decreased until adenectomy (Fig. 3A), but 6 patients presented with an atypical PTH surge during adenoma preparation (Fig. 3B).

Interestingly, up to one-half of the patients with a decrease in PTH during adenoma preparation (n = 14) already exhibited a PTH <50% of the preoperative baseline value at the time of adenectomy (Table 2). Within 10 min, all 14 of these patients fulfilled the criteria for cure (PTH decrease >50% of preoperative baseline value), irrespective of the assay. The results from the six patients with an atypical PTH surge during preparation differed. The DPC PTH assay was the only test that predicted cure at 10 min for all patients. It took 15 min until the Roche PTH was 50% of the preoperative baseline in patients with a transient PTH surge. The Nichols assay failed to predict a cure at 15 min in one case, and samples had to be obtained at later time points to confirm surgical success.

In contrast to the measured PTH values, the calculated residual PTH was always <50% of the preoperative baseline, apparently serving as a more precise criterion for cure (Fig. 4). Furthermore, residual PTH had dropped below the upper reference limit (65 ng/L PTH) for all but two patients with the Nichols assay (74 and 79 ng/L) and in one of them with the Roche test (89 ng/L). Results were available from these two patients at later time points. When these results were added for recalculations, all residual PTH concentrations were within the reference interval (not shown). Cure of all patients was confirmed by their 1-year outcome of normocalcemia.

### Table 2. Number of patients with PTH <50% of preoperative baseline values at indicated time points.

<table>
<thead>
<tr>
<th>Time after adenectomy, min</th>
<th>Nichols</th>
<th>DPC</th>
<th>Roche</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7 (0)</td>
<td>6 (0)</td>
<td>6 (0)</td>
</tr>
<tr>
<td>5</td>
<td>14 (0)</td>
<td>14 (2)</td>
<td>14 (0)</td>
</tr>
<tr>
<td>10</td>
<td>14 (2)</td>
<td>14 (6)</td>
<td>14 (3)</td>
</tr>
<tr>
<td>15</td>
<td>14 (5)</td>
<td>14 (6)</td>
<td>14 (6)</td>
</tr>
</tbody>
</table>

*a Values in parentheses indicate patients with a PTH surge until adenectomy (compare with Fig. 3; in 14 patients PTH decreased and in 6 patients PTH increased until adenectomy)."

**Discussion**

Rapid intraoperative PTH monitoring serves as a “biochemically frozen section” (2) and has become an important prerequisite for minimally invasive parathyroidectomy. Major experience has been gathered with the manual Nichols test that was compared with automated assays from DPC and Roche. In principle, the entire
analytical system may be transported by trolley to the operating theater, but in this study the DPC analyzer was used only in the main laboratory. We recommend direct contact between surgical and analytical teams; this minimizes the time for transporting blood samples and improves communication.

Methodologic comparison among the three PTH assays produced good overall correlation; however, when we calculated regression lines for each patient, remarkable individual deviations appeared. To investigate the clinical relevance of these differences, we used two approaches: calculation of PTH elimination kinetics and evaluation of criteria to predict cure by intraoperative PTH monitoring.

We retrospectively applied two kinetic models to the data obtained: Model A had already been published by Libutti et al. (13) but did not fit properly. Therefore, we established an alternative procedure (model B). Both models are based on an ideal exponential decay, super-imposed by an additive value that is either a function of time ($\Delta c_i$; model A) or a constant ($\mu_i$; model B). Model A describes fast relief of healthy glands from total PTH suppression after adenectomy because of an unconfirmed assumption that the relief mathematically depends on the same rate constant ($k$) as the adnomatous PTH decay. Such a “swing-off/swing-on” mechanism seems debatable during the short time frame of surgery. Similarly not verified, model B assumes a constant contribution of PTH from suppressed healthy glands, which may be a more likely condition during surgery. Despite the different suppositions, both models yield identical half-lives and residual concentrations in an ideal setting, but they differ in $c_0$ and the “true” PTH decay curve of the adenoma (Fig. 1).

In model A, the curve function was solved by iterations, assuming three error-free measurements (a minimum of data sets to calculate a curve); because of this rigidity, some calculations yielded nonsensical results. This model could not be used in cases without uniform reactions in a different manner because commercially intact PTH assays may detect $1 \text{–} 84$ fragments ($20 \text{–} 21$).

A major clinical question that presents itself is the problem as to which PTH concentration, either PTH at $t = 0$, it is a different thing to estimate a sufficient PTH decrease. For several reasons, when judging the PTH decrease, the preoperative PTH value should serve as the reference when calculating the 50% decrease within 10 min. No standard procedure is recommended in the literature. Although for kinetic calculations the PTH at adenectomy was shown to be superior to the concentration at $t = 0$, it is a different thing to estimate a sufficient PTH decrease. For several reasons, when judging the PTH decrease, the preoperative PTH value should serve as the baseline:

Case 1 (14 patients; Table 2). The decrease in PTH from the preoperative baseline to adenectomy indicates that the vessels of the affected gland have indeed been clamped.
before excision. Especially if PTH at adenectomy is $<50\%$ and within the reference interval, cure is indicated. PTH at 5 min should serve for confirmation, and additional monitoring may be omitted. If the PTH at excision is $>50\%$, monitoring is required to exclude multiple gland disease. Kinetic calculations are helpful for estimating the residual PTH concentration and the patient’s clearance rate. A slow decrease in PTH may also be caused by a prolonged half-life and not necessarily by additional hyperfunctioning glands. If the residual PTH is within the reference interval, monitoring may be stopped.

**Case 2 (6 patients; Fig. 3B).** Increasing PTH from the preoperative baseline to adenectomy originates from squeezing of the glands or the adenoma by surgical manipulations. This causes a rapid and sometimes very high efflux of PTH, which thereafter decreases (our own unpublished observation). Such a manipulation complicates the assessment of monitoring because there is an additional overlay by the PTH decay curve of the previously squeezed gland. Most likely, the rate constants ($k$) are identical with reference to the PTH decay from the manipulated gland as well as from the resected adenoma. Thus, assuming a constant PTH contribution from the residual gland ($\rho$), the measured PTH is: $c_m = (c_0 + c_S)e^{-kt} + \rho$, where $c_0$ is the PTH from the adenoma at resection and $c_S$ is the contribution from the PTH decay of the manipulated gland at the time of adenectomy. The problem is that the ratio between $c_0$ and $c_S$ is unknown and $c_0 + c_S$ is the starting concentration observed when monitoring at adenectomy. In other words, by referring only to the concentration at adenectomy, it is uncertain whether the PTH decrease reflects resection of the adenoma alone (assuming that the PTH of the manipulated gland has already come back to its presqueezed value), both PTH sources (unknown $c_0/c_S$ ratio), or the manipulated gland alone (assuming that by mistake the adenoma was left in situ and a gland was removed).

Thus, for clinical judgement, the preoperative baseline is necessary (a) to be able to distinguish between the effects of surgical preparations such as clamping of vessels or unintentional squeezing of parathyroids, (b) for estimating cure [conceivably PTH at the end of monitoring has to be much lower than before the start of the operation, i.e., $<50\%$ of baseline (1)], and (c) for estimating the duration of monitoring. Prolonged monitoring may be necessary in cases with an atypical PTH surge until adenectomy (case 2) if the criterion (1) of PTH $<50\%$ within 10 min is missed, as shown in Table 2. Comparing results of intraoperative monitoring, kinetic calculation of residual PTH may help to reduce the need for expanded monitoring. Although in one case PTH at 15 min was still $>50\%$ (Table 2), all assays provided a residual PTH $<50\%$ (Fig. 4). Currently we are testing a large group of patients to determine whether calculating the residual PTH from bland glands, which we propose to be normal to below-normal values, may replace the recommended "$50\%$ criterion” (1). A more detailed discussion on the pitfalls in PTH monitoring is beyond the scope of this report and will be published elsewhere.

In conclusion, monitoring of the PTH decay appeared to be influenced by surgical manipulations during the more difficult adenoma preparation in minimally invasive parathyroidectomy. Data reduction by kinetic calculations may support assessments by providing additional information on individual half-lives and residual PTH. Kinetic estimations by interpolation of at least four data sets (model A), which sometimes yield incongruous results because of deviating measurements. Preoperative baseline PTH is inadequate for kinetic calculations and must not be used as a surrogate for the concentration at adenectomy. On the other hand, estimation of cure calls for a relation to the PTH before the treatment starts (preoperative baseline). Understandably, the PTH at the end of monitoring has to be much lower than the preoperative baseline value. In our opinion, it was beneficial to monitor at the site of surgery to keep short distances between sampling as well as analyzing and transporting information. Although interindividual methods of comparing as well as calculating half-life and residual PTH concentrations revealed differences among the three assays, in clinical practice they may be neglected. Because multiple intraoperative measurements are necessary (routinely we do at least five), costs and efficiency may be the main criteria when choosing an automated assay, and it seems advantageous to use the same chemistry as for routine PTH analyses.

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**References**


