Hematocrit of the Human Cranial Blood Pool

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Since the hematocrit of arteriolar and capillary blood is substantially lower than that found in larger vessels, the mean hematocrit of total organs will be lower than the large vessel hematocrit, particularly in organs, such as human brain, that contain very rich capillary beds. This has been demonstrated in many tissues.

It is the purpose of this article to describe a basic technique for determining safely and simply the mean hematocrit of the human cranial blood pool. The method utilizes the separate and sequential intravenous administration of gamma-labeled red cells and plasma.

Methods

Before the subject is studied, 20 ml of blood are withdrawn, labeled with Cr\textsuperscript{51} chromate (Na\textsubscript{2}Cr\textsuperscript{51}O\textsubscript{4}), and washed twice with saline. A 5 ml venous specimen is also drawn for a centrifuged hematocrit (Hct\textsubscript{v,creat}). No premedication is administered.

The subject is placed supine with his head positioned between collimated, shielded, thallium-activated sodium iodide crystals. The arrangement of crystals relative to the head is shown in figure 1. The crystals measure 15 x 5 x 3.5 cm and are arranged with their long axes approximately parallel to the main mass of the cerebral hemispheres. The head is maintained in fixed position relative to the crystals by means of earplugs fixed to the lead shielding. A plastic rod with a 2.5 cm diameter, fixed in relation to the lead shielding, rests on the bridge of the nose.

By utilizing thick lead correcting plates midway between the crystals and the lateral surfaces of the head (fig. 1), the efficiency of the detection system for radiation originating anywhere in the cranial cavity is made almost uniform. In a water-filled commercial phantom containing a human skull, a point source of I\textsuperscript{131} produces a count-rate uniform within 10% for most points within the cranial cavity (fig. 2). Such a uniformly efficient system allows accurate quantification of the total cranial content of a gamma emitter, because the count rate is independent of the distribution of radio-isotope within the field of detector sensitivity. Although these efficiency distribution measurements were made with I\textsuperscript{131}, it is assumed that they are very similar for the gamma radiation of Cr\textsuperscript{51} also used in these studies since the characteristics of Cr\textsuperscript{51} gamma radiation resemble closely those of I\textsuperscript{131}. The quantum efficiency for I\textsuperscript{131} with this cranial detection system, as used here, is approximately 1%.

A total of six measurements is made during the testing procedure, three from the cranial blood pool (counts 1, 3, 5) and three from venous specimens (counts 2, 4, 6). Blood samples are drawn from an antecubital vein several mm in diameter. A low pressure tourniquet is used. A four-minute background cranial count (count 1) is obtained. A 12 ml antecubital blood specimen is withdrawn into a heparinized syringe as a peripheral venous background sample (count 2). Twenty ml of the patient’s blood labeled with Cr\textsuperscript{51} are injected intravenously during a 30 to 45-second interval. Forty microcuries of Cr\textsuperscript{51} will approximately triple the cranial detector background count rate. Four minutes...
Diagram showing the arrangement of broadly collimated scintillation crystals in relation to head as seen from the front. The 4 mm thick lead correction plates (indicated by arrows) have lateral dimensions one-half the face dimensions of the crystals. The correcting plates placed between crystals and subject reduce the counting efficiency but more so for superficially positioned isotope. These plates present a larger solid angle to superficial isotope than to more deeply located isotope, resulting in a greater absorption of surface radiation. This corrects partially for the inverse square law and internal absorption which ordinarily cause an increased efficiency for superficial isotope. The counts shown here are from a point source moved along the base line of the graph on a line paralleling the coronal plane.

Diagram illustrating that the efficiency of detection of $^{131}$ gamma radiation becomes almost uniform when the outputs of both crystals shown in figure 1 are summed. These data were derived by moving a point source about within a water-filled radiological phantom containing a skull. Values at a point near the middle of the cranial cavity are chosen arbitrarily to represent 100%. This distribution is considerably more uniform than found before introducing correcting plates shown in figure 1. With such uniform efficiency, the count rate becomes nearly independent of location of radiation source.

Circulation Research, Vol. XVII, December 1965
Example of count-rate obtained from the cranium after intravenous injections of red cell and plasma labels. Arrows show timing of withdrawal of venous specimens midway during cranial count periods.

plasma volume in the field of the cranial detector. In the middle of this four-minute plasma counting period, a 12 ml antecubital venous plasma label specimen (count 6) is drawn from the arm opposite the injection site, into a heparinized syringe.

Since the relationship between the cranial and blood counts is used in this technique, total mixing is not required. It is necessary only that both venous and cranial counts represent tracer distribution at the same time. The mixing time is kept short to minimize the total time the subject is required to remain stationary and to minimize head movement. A short plasma label mixing time minimizes loss of this label from the plasma pool.

Ten grams of each blood specimen are put into 2.5 cm diameter test tubes. To minimize settling of the red cells into the deeper, more efficient portions of the well counting crystal, 0.3 cc of saponin* solution is mixed with each of the three antecubital venous specimens. A 20,000 preset count is performed on each specimen. These blood specimens represent combinations of counts: the background count (2), the background count plus red cell volume count (4), and the background count plus red cell volume count plus plasma volume count (6).

From these three venous specimens (2, 4, and 6) two net values are derived, one net value for the venous red cell volume and another net value for the venous plasma volume. The net venous red cell volume (R.C.V.v) is calculated by subtracting the count obtained for the background venous sample (2) from the second antecubital sample count (4). The net plasma count (P.V.v) is obtained by subtracting the second blood specimen count (4) from the third blood specimen count (6).

The three cranial counting periods (fig. 3) represent separate and successive additions of counts: the cranial detector background count (1), the background plus red cell volume count (3), and the background plus red cell volume plus plasma volume count (5). From these three sequential counts, two net values are derived, one proportional to the cranial red cell volume and the other value for the cranial plasma volume. The net red cell volume (R.C.V.cr) is calculated.

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*E. Berghausen Chemical Company, Cincinnati, Ohio.
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by subtracting the background count (1) from count (3) obtained after red cell label injection and distribution. The net plasma count (P.V.cr) is obtained by subtracting the second cranial count (3) taken after the red cell label distribution from the third cranial count (5) obtained after plasma label injection and distribution.

From the net red cell volume (R.C.V.cr) and plasma volume (P.V.cr) in the cranium, and from the net red cell volume (R.C.V.v) and plasma volume (P.V.v) in the venous specimens, the relationship between the hematocrit of the cranial blood pool (Hct.cr) and the venous hematocrit (Hct.v) is derived. Since we assume an equal representation of all portions of the cranial blood pool in our external counts, this will be a mean value for the entire cranial pool. The mean value for Hct.cr/Hct.v in the cranial portion of the head in this study was 0.84. The cranial blood pool hematocrit (Hct.cr) is derived from Hct.cr/Hct.v and the centrifuged hematocrit (Hct.v.cent.) taken previous to the procedure.

Hematocrit (Hct) is here defined as:

\[
Hct = \frac{R.C.V.}{R.C.V. + P.V.} \times 100 \tag{1}
\]

where \( Hct \) = hematocrit.

\( R.C.V. \) = red cell volume.

\( P.V. \) = plasma volume.

The ratio of cranial blood pool hematocrit (Hct.cr) to venous hematocrit (Hct.v) is:

\[
\frac{Hct_{cr}}{Hct_{v}} = \frac{\frac{R.C.V._{cr}}{R.C.V._{cr} + P.V._{cr}}}{\frac{R.C.V._{v}}{R.C.V._{v} + P.V._{v}}} \tag{2}
\]

R.C.V.cr = net red cell count from the cranial detector.

P.V.cr = net plasma count from the cranial detector.

R.C.V.v = net red cell count from the venous blood specimen.

P.V.v = net plasma count from the venous blood specimen.

The mean value of the cranial to venous hematocrit ratio times a centrifuged venous hematocrit yields an absolute derived value for the cranial blood pool hematocrit (Hct.cr).

\[
Hct_{cr} \times \frac{Hct_{v, cent.}}{Hct_{v}} = Hct_{cr} \tag{3}
\]

Hct cr is the same as Hct v,cent. but is never obtained directly in this technique. Such a measurement would require a knowledge of total red cell and plasma pool volumes and the absolute amounts of the administered labels. Its value is not required here.

The venous hematocrit (Hct v,cent.) of equation 3 is obtained by centrifugation of a venous specimen drawn separately for the purpose prior to the beginning of the test. This oxalated specimen is spun at 2500 rpm for 30 minutes in a Wintrobe tube.

Since only the ratios of net red cell and net plasma counts from the cranial detector samples are utilized in this relative hematocrit calculation, the absolute amount of the administered radioisotope need be approximate only and is determined here by the need to obtain between two and three times cranial detector background count after the Cr\(^{51}\) red cell administration, and to approximately triple this red cell count to measure accurately the Cr\(^{51}\) plasma count. With 40 microcuries of Cr\(^{51}\) red cells, a count of approximately 30,000 is obtained in four minutes. With the subsequent administration of 80 microcuries of Cr\(^{51}\) albumin, approximately 100,000 counts are obtained in four minutes. The counting linearity of this detection system is such that no correction need be made for nonlinearity at this count rate, since the resolution of system pulse pairs is approximately 25 microseconds. Every fourth pulse representing a gamma ray of greater than 200 kev energy level is recorded on magnetic tape. Cranial counts are obtained from the subsequent playback of this magnetic tape into a rate meter, chart recorder, and scaler (fig. 3).

Cr\(^{51}\) human albumin is not generally available commercially. Because of this, an alternate technique was evaluated in which \( I^{123} \) human serum albumin (HSA) was substituted for Cr\(^{51}\) albumin. The technique was similar to that already described, except that 10 microcuries of HSA was used in place of 80 microcuries of Cr\(^{51}\) albumin.

The utilization of Cr\(^{51}\) as the label for both the red cell and the plasma compartments simplifies the calculation of cranial hematocrit (Hct cr), because no correction need be made for different efficiencies of the external cranial detector and the well counter. Although the major gamma emission of \( I^{123} \) (82% at 364 kev) is similar to the gamma emission of Cr\(^{51}\) (9% at 324 kev), \( I^{123} \) produces 9% at 638 kev gamma radiation. This higher energy radiation of \( I^{123} \) albumin plus the slightly different major gamma emission of iodine results in a difference of gamma radiation characteristics sufficient to warrant a substantial correction factor in this modified Cr\(^{51}\) albumin technique.

To correct for the difference in counting efficiencies of the cranial detection system and the well counter for Cr\(^{51}\) and \( I^{123} \), two test solutions were made in test tubes with 2.5 cm diameters each containing 10 grams of saline.
One test tube contained 0.1 microcurie of I\(^{131}\), and the other 0.5 microcurie of Cr\(^{51}\). A commercial water-filled phantom containing a human skull was placed in position between the detectors. By means of a hole in the forehead of the phantom, each test tube was counted while submerged in the middle of the cranial cavity. The same two test tubes were then each counted in the well counter.

From these counts (phantom and well counter) it was determined that the well counter was 26% more efficient for Cr\(^{51}\) than for I\(^{131}\). As a result of this difference, it was necessary to introduce a correction factor for the net venous red cell or net plasma volume in equation 3. To equalize the cranial well counter and the external blood specimen well counter, either (R.C.V.\(_r\)) could be reduced by a factor of 0.74 or (P.V.\(_r\)) could be increased by a factor of 1.33. It was elected arbitrarily to correct R.C.V.\(_r\). Equation 2 becomes for our apparatus:

\[
\frac{R.C.V.\text{cr}}{Hct_r} = \frac{R.C.V.\text{cr} + P.V.\text{cr}}{0.74 \times R.C.V.\text{v} + P.V.\text{v}}
\]

For collimator arrangements and threshold settings differing from those described here, the value of this correction factor would differ from that used in this study.

### Results

Thirty-two cases were studied by the above techniques, sixteen with Cr\(^{51}\) albumin (table 1) and sixteen with I\(^{131}\) RISA (table 2). The mean value of the cranial to venous hematocrit ratio \(\frac{Hct_{cr}}{Hct_r}\) is 0.84 using Cr\(^{51}\) albumin and 0.84 using I\(^{131}\) RISA. This ratio was not found to be unusual in a polycythemic patient (MC) or in an anemic patient (ED) included in this study (table 1).

### Discussion

The concept of measurement of red cell to plasma volume distribution ratio in the brain blood pool by an external, uniform efficiency gamma detector has been described.\(^7\) It is generally recognized that the hematocrit of circulating blood is reduced in small blood vessels.\(^1\) Accordingly, the hematocrit of individual organs and of the total blood pool of entire organisms is measurably lower than the hematocrit derived by the centrifugation of a drawn large vessel blood specimen. The total human body blood pool hematocrit is approximately 0.91 times the venous hematocrit.\(^8,9\) Since many large vessels are included in the total body blood pool, it is to be anticipated that organs (other than spleen)\(^8\) containing a large capillary blood content will usually show a sub-

### Table 1

Results Obtained in Sixteen Subjects Studied with Cr\(^{51}\) Red Cell and Cr\(^{51}\) Albumin

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Venous hematocrit (centrifuged) %</th>
<th>Brain/venous hematocrit ratio</th>
<th>Brain hematocrit</th>
</tr>
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<tbody>
<tr>
<td>1—FG</td>
<td>38</td>
<td>Normal</td>
<td>44.0</td>
<td>.81</td>
<td>35.6</td>
</tr>
<tr>
<td>2—HJ</td>
<td>63</td>
<td>Normal</td>
<td>42.0</td>
<td>.82</td>
<td>34.4</td>
</tr>
<tr>
<td>3—SC</td>
<td>62</td>
<td>Cerebrovascular disease</td>
<td>37.0</td>
<td>.82</td>
<td>30.3</td>
</tr>
<tr>
<td>4—BA</td>
<td>63</td>
<td>Cerebrovascular disease</td>
<td>44.0</td>
<td>.83</td>
<td>36.5</td>
</tr>
<tr>
<td>5—AC</td>
<td>64</td>
<td>Cerebrovascular disease</td>
<td>48.0</td>
<td>.92</td>
<td>47.8</td>
</tr>
<tr>
<td>6—CR</td>
<td>48</td>
<td>Cerebrovascular disease</td>
<td>48.0</td>
<td>.79</td>
<td>37.9</td>
</tr>
<tr>
<td>7—KJ</td>
<td>36</td>
<td>Normal</td>
<td>43.0</td>
<td>.81</td>
<td>34.8</td>
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<tr>
<td>8—MN</td>
<td>37</td>
<td>Alcoholic polyneuritis</td>
<td>37.0</td>
<td>.84</td>
<td>31.1</td>
</tr>
<tr>
<td>9—ML</td>
<td>40</td>
<td>Normal</td>
<td>53.0</td>
<td>.81</td>
<td>42.9</td>
</tr>
<tr>
<td>10—SS</td>
<td>45</td>
<td>Alcoholic polyneuritis</td>
<td>40.5</td>
<td>.88</td>
<td>35.6</td>
</tr>
<tr>
<td>11—MK</td>
<td>30</td>
<td>Prog. muscular atrophy</td>
<td>41.5</td>
<td>.90</td>
<td>37.3</td>
</tr>
<tr>
<td>12—FW</td>
<td>54</td>
<td>Cerebrovascular disease</td>
<td>43.5</td>
<td>.88</td>
<td>35.2</td>
</tr>
<tr>
<td>13—GR</td>
<td>38</td>
<td>Idiopathic epilepsy</td>
<td>40.0</td>
<td>.88</td>
<td>35.2</td>
</tr>
<tr>
<td>14—WC</td>
<td>37</td>
<td>Normal</td>
<td>40.0</td>
<td>.91</td>
<td>36.4</td>
</tr>
<tr>
<td>15—MC</td>
<td>58</td>
<td>Physiologic polycythemia</td>
<td>64.5</td>
<td>.89</td>
<td>57.4</td>
</tr>
<tr>
<td>16—ED</td>
<td>49</td>
<td>Pernicious anemia</td>
<td>17.0</td>
<td>.82</td>
<td>13.9</td>
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</table>

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TABLE 2
Results Obtained in Sixteen Subjects Studied With Cr\textsuperscript{51} Red Cell and RISA

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Venous hematocrit (centrifuged)</th>
<th>Brain/venous hematocrit ratio</th>
<th>Brain hematocrit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1—CP</td>
<td>33</td>
<td>Normal</td>
<td>47.0</td>
<td>0.82</td>
<td>38.5</td>
</tr>
<tr>
<td>2—LM</td>
<td>32</td>
<td>Multiple sclerosis</td>
<td>44.0</td>
<td>0.82</td>
<td>36.0</td>
</tr>
<tr>
<td>3—CK</td>
<td>41</td>
<td>Idiopathic epilepsy</td>
<td>47.0</td>
<td>0.84</td>
<td>39.5</td>
</tr>
<tr>
<td>4—DF</td>
<td>49</td>
<td>Alcoholic polyneuritis</td>
<td>39.0</td>
<td>0.80</td>
<td>31.2</td>
</tr>
<tr>
<td>5—RI</td>
<td>33</td>
<td>Post-traumatic encephalopathy</td>
<td>47.0</td>
<td>0.91</td>
<td>42.8</td>
</tr>
<tr>
<td>6—CC</td>
<td>45</td>
<td>Hypothyroidism</td>
<td>42.0</td>
<td>0.93</td>
<td>39.1</td>
</tr>
<tr>
<td>7—DP</td>
<td>65</td>
<td>Retrobulbar neuritis</td>
<td>43.0</td>
<td>0.90</td>
<td>38.7</td>
</tr>
<tr>
<td>8—DS</td>
<td>62</td>
<td>Cerebrovascular disease</td>
<td>46.5</td>
<td>0.91</td>
<td>42.3</td>
</tr>
<tr>
<td>9—ES</td>
<td>64</td>
<td>Idiopathic epilepsy</td>
<td>44.0</td>
<td>0.86</td>
<td>37.8</td>
</tr>
<tr>
<td>10—AF</td>
<td>65</td>
<td>Cerebrovascular disease</td>
<td>44.0</td>
<td>0.81</td>
<td>35.6</td>
</tr>
<tr>
<td>11—CK</td>
<td>35</td>
<td>Normal</td>
<td>44.0</td>
<td>0.86</td>
<td>37.8</td>
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<tr>
<td>12—EB</td>
<td>44</td>
<td>Normal</td>
<td>43.0</td>
<td>0.88</td>
<td>38.1</td>
</tr>
<tr>
<td>13—CD</td>
<td>57</td>
<td>Retrobulbar neuritis</td>
<td>45.5</td>
<td>0.84</td>
<td>38.2</td>
</tr>
<tr>
<td>14—CA</td>
<td>54</td>
<td>Normal</td>
<td>41.0</td>
<td>0.88</td>
<td>38.1</td>
</tr>
<tr>
<td>15—LB</td>
<td>48</td>
<td>Normal</td>
<td>48.0</td>
<td>0.80</td>
<td>38.4</td>
</tr>
<tr>
<td>16—CB</td>
<td>38</td>
<td>Normal</td>
<td>38.0</td>
<td>0.85</td>
<td>32.3</td>
</tr>
</tbody>
</table>

stantially lower hematocrit than the mean value 0.91 for the entire body.

The finding presented here, of a mean cranial hematocrit 0.84 times the venous hematocrit seems, therefore, to be reasonable. This value is in general agreement with the hematocrit of most other organs derived by other experimental means.\textsuperscript{2-5} This finding represents presumably, and for the most part, the characteristics of the brain blood pool but some small contribution from scalp, skull, and meninges is also included in the field of the cranial detector. The human brain is ideally suited to such total organ measurements since it constitutes the major portion of tissue in the head rostral to the floor of the cranial cavity. As a result of this, measurement of total tissue content rostral to the floor of the cranium will be highly representative of brain tissue. The isolation and external counting of brain isotope content will be less applicable in other species because the values for brain are obscured more by those of other non-neural tissues.

Since the hematocrit value derived for the total organ is lower than the hematocrit in the large vessels going to and coming from the organ, the mean transit time of red cells through the organ is presumably faster than the mean transit time of plasma. This has been demonstrated in other organs.\textsuperscript{10-12} The reduction of total organ red cell to plasma ratio will be proportional to the difference in plasma and red cell mean organ transit times. This red cell to plasma ratio reduction will approximate the reduction in hematocrit defined in equation 1.

To corroborate our finding of a 16% reduction of total brain organ hematocrit, a separate injection into the carotid artery of labeled red cells and plasma was performed on patient EB of table 2. In this case, a 3 ml volume of the patient's blood, containing 25 microcuries of Cr\textsuperscript{51} labeled red cells, was injected rapidly into the common carotid artery through a 20-gauge needle. Injection time was less than 0.5 second. A similar injection of 5 microcuries of I\textsuperscript{131} RISA was performed through the same needle, with care taken to mix the original radioisotope in 0.25 ml of saline and to withdraw arterial blood back into the syringe sufficient to make 3 ml of total volume prior to injection. In this way the hematocrit of the injected label was made nearly identical to arterial blood for both red cell and plasma labels. As shown in figure 4, the labeled red cells pass through the cranial blood pool substantially faster...
Example of cranial count after abrupt sequential injection into the common carotid artery of red cell and plasma labels. Red cell label passes out of the pool more rapidly than the plasma label. Care was taken to equalize the hematocrit of each injected specimen.

than does the labeled plasma. The mode circulation time through the cranial blood pool, represented here by the maximal rate of fall of the cranial count rate, is approximately 15% shorter with the red cell label than with plasma. This agrees in general with the results of Crane et al. who showed a similar disparity in the red cell and plasma transit times through the heads of dogs.

We consider this only as crude corroboration of the reduction of hematocrit found by the intravenous technique under discussion here. The determination of the maximum rate of fall of brain blood pool isotope content will provide the most common (mode) circulation time through the pool. This will be somewhat shorter than the mean circulation time through the pool. This determination cannot be made with great precision because the effective counting interval required to define accurately such a rapidly changing count rate is very short. As a result, statistical noise becomes a limiting factor despite the availability of rather high count rates from our apparatus.

Utilizing a carotid and jugular sampling technique, following antecubital venous injection of red cells and plasma labels, Larsen and Lassen established a hematocrit of the cranial blood pool below the large vein value. Their mean value for $\text{Hct}_{cr}/\text{Hct}_v = 0.93$. These workers cannulated the carotid arteries and jugular veins to establish the relative difference in flow rates through human brain of the red cell and plasma compartments. From these data the volumes of red cell and plasma in brain were calculated.

This technique makes it possible to assess atraumatically, and with considerable precision, the disparity of behavior of red cells
and plasma in the brain circulation. Since there is a relationship between vessel size, flow rate, shear properties of blood and hematocrit, this technique could provide data correlating these factors with clinical abnormalities.

Summary
A technique is described utilizing the separate injection of gamma-labeled red cells and plasma, with subsequent measurement of the amount of each label found in the cranial portion of the head and in venous blood specimens. By this means the relationship between the hematocrit of the cranial blood pool and venous blood is determined. In the basic technique, $^{51}$Cr is used separately and sequentially as the label for both red cells and plasma. A modification of this technique using $^{131}$I human serum albumin is described also. Only antecubital venipuncture for injection and sampling was utilized. The mean hematocrit of the human cranial blood pool was found to be 0.84 times the venous hematocrit by both dual tracer methods. This technique should be applicable to other organs. The distribution ratios of any gamma emitters in brain and blood should be similarly measurable.

Acknowledgment
The authors are indebted to Dennis D. Patton, M.D. and Benedict Cassen, Ph.D. for their many valuable suggestions.

References
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Circ Res. 1965;17:532-539
doi: 10.1161/01.RES.17.6.532
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1965 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

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