

# Regional Scalp Block for Postcraniotomy Analgesia: A Systematic Review and Meta-Analysis

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**BACKGROUND:** Up to two-thirds of patients report moderate to severe surgical site pain after craniotomy procedures, and there is understandable reluctance to manage these symptoms with systemic opioids that may impair neurological assessment. Furthermore, there is a lack of consensus and evidence concerning alternative analgesia strategies for cranial neurosurgery. Regional scalp block (RSB) is an established technique that involves infiltration of local anesthetic (LA) at well-defined anatomical sites targeting the major sensory innervation of the scalp. However, the efficacy of RSB in reducing postoperative pain remains unclear. In this study, we sought to systematically identify and review randomized controlled trials (RCTs) of RSB and synthesize an overall estimate of efficacy in a quantitative meta-analysis.

**METHODS:** Medline, EMBASE, and the Cochrane Central Register of Controlled Trials databases were searched for all RCTs evaluating the effect of RSB on postoperative pain after craniotomy. Titles, abstracts, and papers were reviewed independently by 2 authors against predefined inclusion criteria. Two authors independently assessed the quality of included studies and extracted data on patient-reported pain scores, other analgesia requirements, and complications of RSB. Pain scores were scaled to a common 0 to 10 interval with higher scores indicating more severe pain. Meta-analysis of the pooled treatment effect was performed with a random-effects inverse-variance weighted model; heterogeneity was quantified with the  $I^2$  statistic.

**RESULTS:** The literature search identified 138 unique citations, from which 7 RCTs with a total recruitment of 320 patients met the inclusion criteria. All studies used standard LA drugs (lido-caine, bupivacaine, or ropivacaine); in 3 studies, LA was combined with epinephrine. In 3 studies, RSB was performed preoperatively; in the other 4 studies, it was administered postoperatively after wound closure. No complications attributable to RSB were reported. Meta-analysis found a pooled reduction in pain score at 1 hour postoperatively ( $N = 5$  studies; mean difference,  $-1.61$ ; 95% confidence interval,  $-2.06$  to  $-1.15$ ;  $P < 0.001$ ;  $I^2 = 0\%$ ). Subgroup analysis of preoperative RSB showed significant reduction in pain scores at 2, 4, and 6 to 8 hours after surgery whereas postoperative RSB was associated with significant reduction in pain scores at 2, 4, 6 to 8 and 12 hours assessments. There was also an overall reduction in the opioid requirements over the first 24 hours postoperatively, although with significant heterogeneity among the studies ( $N = 6$  studies; standardized mean difference,  $-0.79$ ; 95% confidence interval,  $-1.55$  to  $-0.03$ ;  $P = 0.04$ ;  $I^2 = 86\%$ ).

**CONCLUSION:** Published RCTs of RSB are small and of limited methodological quality but meta-analysis shows a consistent finding of reduced postoperative pain. This evidence supports the use of RSB for patients undergoing craniotomy. (Anesth Analg 2013;116:1093–102)

Around two-thirds of patients report moderate to severe pain after craniotomy in prospective studies, and surveys of analgesia management indicate there is little consensus on best practice.<sup>1,2</sup> Furthermore, there is specific concern that providing pain relief with systemic opioids in the postoperative period after neurosurgical procedures may cloud neurological assessment and obscure early signs of

intracranial complications.<sup>3</sup> For this reason, regional blockade of sensory innervation to the scalp has become a frequently used adjunct to systemic analgesia for craniotomy procedures.

The standard regional scalp block (RSB) technique is performed by targeted infiltration of 2 to 3 mL of local anesthetic (LA) solution at multiple sites with a 23 to 25G needle<sup>4–6</sup> (Fig. 1; see Kemp et al.<sup>6</sup> for an in-depth discussion). First, the supraorbital and supratrochlear nerves are blocked as they emerge from the orbit with LA infiltrated above the eyebrow. The auriculotemporal and great auricular nerves are each blocked with LA injected anterior and posterior to the ear, respectively, approximately at the level of the tragus. Finally, the greater, lesser, and third occipital nerves are blocked collectively with a single injection of LA along the superior nuchal line at the midpoint between inion and mastoid process. Optionally, the zygomaticotemporal nerve can also be blocked by an injection of LA lateral to the orbit. RSB may be performed either unilaterally or bilaterally, as required; for limited

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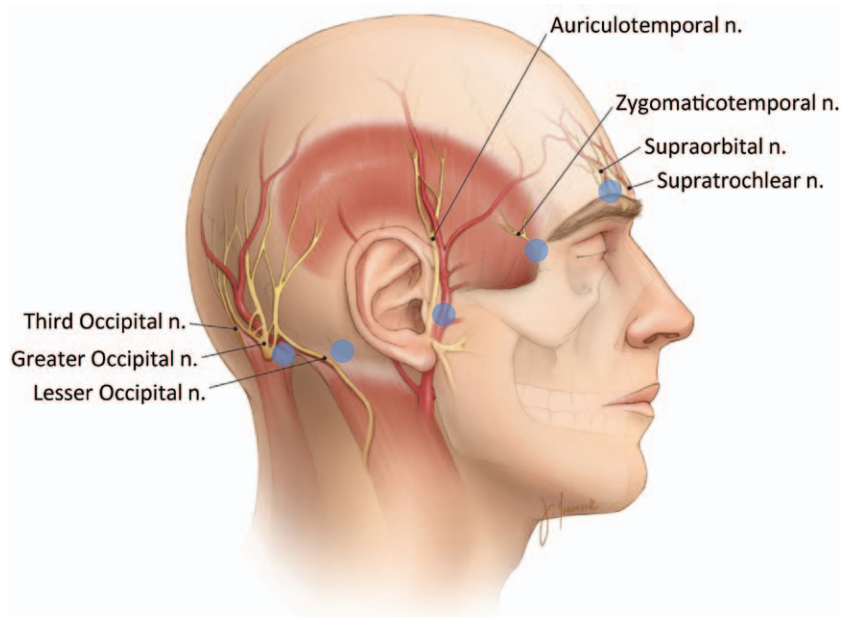
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**Figure 1.** Anatomy of the principal sensory innervation to the scalp. The regional scalp block (RSB) technique involves 4 to 5 injections of local anesthetic at sites indicated by the blue dots, targeting the nerves labeled (see text for details). This figure is adapted from Figure 2 in Kemp 3rd WJ et al.<sup>6</sup> under the Creative Commons Attribution License.

exposures, only a subset of the injections may be administered. In addition to analgesia, RSB has ancillary potential benefits including attenuating autonomic cardiovascular responses to skull pinning, incision, and craniotomy.<sup>5</sup>

Although there are several observational and randomized studies of RSB in the literature, they have generally involved relatively small sample sizes and have drawn differing conclusions as to the analgesic efficacy of the technique. Thus, despite widespread use of perioperative RSB, the strength of evidence supporting this practice is unclear. The objective of this study was to conduct a systematic review of RSB for postoperative pain control in adult patients undergoing craniotomy and to synthesize an overall estimate of the treatment effect in a quantitative meta-analysis.

## METHODS

### Trial Selection

This study was conducted and is reported in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).<sup>7</sup> Inclusion criteria were single- or double-blind randomized controlled trials (RCTs) comparing pre- or postoperative RSB against no intervention, systemic analgesia, or other local intervention, in adults undergoing craniotomy, with at least 1 patient-reported pain score as an outcome measure. We considered RSB to be any technique where the region of the scalp to be operated on was blocked by injection of LA around the major innervating sensory nerves, as described originally by Girvin<sup>4</sup> and more recently by Pinosky et al.<sup>5</sup> Studies solely examining the efficacy of infiltrating LA along the planned scalp incision (or postoperatively into the wound margin) were excluded as this was not considered a genuine regional block. However, studies in which RSB was combined together with incision or wound infiltration were included. Studies reporting only physiological variables as outcomes, e.g., heart rate or arterial blood pressure, without any assessment of patients' pain scores, were also excluded.

Search strategies combining medical subject headings (MeSH) or Emtree terms, keywords, and the Cochrane Collaboration RCT filters (Supplemental Table 1 in the Appendix) were applied to the MEDLINE (1946 onwards) and EMBASE (1980 onwards) databases via OvidSP (<https://ovidsp.ovid.com>). The Cochrane Central Register of Controlled Trials (CENTRAL, <http://www.thecochranelibrary.com>) was searched using the MEDLINE strategy with appropriate syntax translation. All searches were performed without language restriction on March 31, 2012 and the results collated and deduplicated in Endnote X4 (Thomson Reuters, New York, NY). Titles and abstracts were screened independently by 2 authors (M.R.G. and A.H.), and the complete reports of any studies potentially fulfilling the inclusion/exclusion criteria were obtained. The full papers were reviewed by 2 authors (M.R.G. and A.H.) for final inclusion.

### Data Extraction

Data from included studies were extracted by 2 authors (M.R.G. and A.H.). The primary outcome of interest was postoperative patient-reported verbal or visual analog pain scores. Where data were reported as median and (interquartile) range, the corresponding authors were contacted to obtain the respective mean and standard deviation; if the results were presented only in graphical form, the relevant data were extracted using ImageJ (v1.45, National Institutes of Health, Bethesda, MD: <http://rsbweb.nih.gov/ij/>). Methodological quality and the risk of bias for each included study were assessed by 2 authors (M.R.G. and A.H.) using the most recent Cochrane Collaboration tool and guidelines.<sup>8</sup>

### Data Synthesis

For the quantitative meta-analysis, mean and standard deviations of the outcome data for each group in each study were entered into Review Manager (RevMan v5.1; The Cochrane Collaboration, Baltimore, MD: <http://ims.cochrane.org/revman>). Pain scores were rescaled to a

Table 1. Included Trials

Study	Year	N	Age (y); mean	Timing	Regional scalp block	Control	Volume (mL)	Duration of surgery (min, mean $\pm$ SD)	Pain score assessments (h)	Rescue analgesia
AYoub et al. <sup>10</sup>	2006	55	18–70; 49.0	Postoperative	Lidocaine 2%/bupivacaine 0.5%	Saline block/morphine 0.1 mg/kg IV	20	RSB: 366 $\pm$ 138 Control: 438 $\pm$ 234	1, 2, 4, 8, 12, 16, 24	Codeine
Bala et al. <sup>11</sup>	2006	40	18–50; 38.5	Postoperative	Bupivacaine 0.5%/epinephrine 1:400,000	Saline/epinephrine 1:400,000	20	RSB: 230 $\pm$ 54 Control: 221 $\pm$ 59	0.5, 1, 2, 4, 6, 8, 12	Tramadol
El-Dahab et al. <sup>12</sup>	2009	80	>65; 70.0	Preoperative	Bupivacaine 0.5%/epinephrine 1:400,000	IV Fentanyl	30	RSB: 276 $\pm$ 43 Control: 258 $\pm$ 49	1, 2, 3, 4, 5, 6	Paracetamol
Gazoni et al. <sup>13</sup>	2008	30	>18; n/a	Preoperative	Ropivacaine 0.5%	No block	30	n/a	1, 2, 4	Opiates <sup>a</sup>
Hernández Palazón et al. <sup>14</sup>	2007	30	18–69; 47.5	Postoperative	Bupivacaine 0.25%/epinephrine 1:200,000	Saline/epinephrine 1:200,000	20	RSB: 281 $\pm$ 80 Control: 247 $\pm$ 48	2, 4, 8, 12, 16, 24	Morphine
Nguyen et al. <sup>15</sup>	2001	30	18–70; 48	Postoperative	Ropivacaine 0.75%	Saline	20	RSB: 283 $\pm$ 146 Control: 292 $\pm$ 90	4, 8, 12, 16, 20, 24, 48	Codeine
Tuchinda et al. <sup>16</sup>	2010	60	16–65; 34.3	Preoperative	(a) Bupivacaine 0.25%/epinephrine 1:200,000 (b) Bupivacaine 0.5%/epinephrine 1:200,000	Saline/epinephrine 1:200,000	21–28	RSB (a): 131 $\pm$ 60 RSB (b): 163 $\pm$ 48 Control: 150 $\pm$ 58	0.5, 1, 1.5, 2, 6, 12, 24	Morphine

n/a = not available in report; RSB = regional scalp block.

<sup>a</sup>Specific opiate not documented in source report; converted to morphine equivalents by original study authors.

standard interval of 0 to 10, and the overall effect size was estimated with a random-effects mean difference (MD) meta-analysis using inverse-variance weighting. When a study included >1 intervention arm compared with a single control group, they were treated as separate trials with the control group divided among the interventions.<sup>8</sup> Data on postoperative opioid consumption were combined in a standardized MD (SMD) random-effects model with inverse-variance weighting. SMD was chosen as the specific opioid and route of administration varied among trials, and calculation of morphine equivalents may have introduced bias. Between-study heterogeneity was quantified with the  $I^2$  statistic. Subgroup (indirect) comparisons were performed by calculating the heterogeneity across subgroups using a fixed-effects inverse-variance weighted approach.<sup>8,9</sup> Publication bias was assessed visually with a funnel plot.

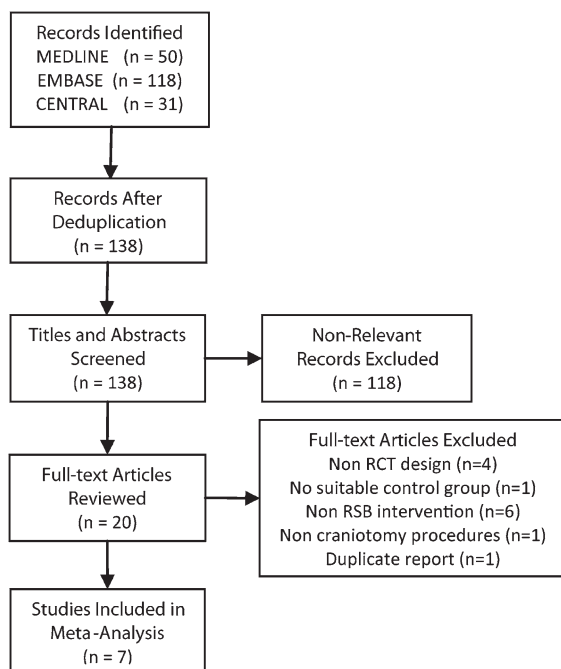
## RESULTS

### Search Results

A total of 138 citations were identified from the literature search (Fig. 2). After screening of titles and abstracts, 118 citations concerning non-RCTs or nonrelevant studies were excluded and 20 full-text reports were retrieved. After detailed review, a further 4 reports were excluded due to non-RCT design, 6 because there was no relevant intervention (either incision infiltration or superior cervical plexus block rather than standard supratentorial RSB), 1 because it lacked a suitable non-RSB control group, and 1 because the patients received stereotactic radiosurgery as opposed to craniotomy. There was also 1 duplicate report. Therefore, 7 reports detailing 7 distinct RCTs of supratentorial RSB, with a total recruitment of 325 patients, were selected for final inclusion in the study.<sup>10–16</sup>

### Description of Included Trials

Key details of the included trials are summarized in Table 1. Five trials included a placebo control arm by performing the RSB with saline (with or without epinephrine),<sup>10,11,14–16</sup> in the remaining 2 trials, RSB was compared with IV fentanyl<sup>12</sup> or no RSB.<sup>13</sup> One trial had a 3-arm design: 2 intervention arms of RSB performed using 0.25% or 0.5% bupivacaine, both with epinephrine, compared against saline and epinephrine as control.<sup>16</sup> In 3 trials, the RSB was performed before skin incision and craniotomy,<sup>12,13,16</sup> whereas in the other 4 trials the RSB was administered after completion of surgery and skin closure but before emergence from general anesthesia.<sup>10,11,14,15</sup> hereafter, these subgroups are referred to as preoperative RSB and postoperative RSB, respectively. In all studies, patients reported pain using a verbal or visual analog score at various time intervals from 30 minutes to 48 hours postoperatively. The majority of studies included assessments at 1 ( $N = 5$  studies), 2 ( $N = 6$ ), 4 ( $N = 6$ ), 12 ( $N = 5$ ), and 24 hours ( $N = 4$ ) after surgery. Because 6 of the studies reported pain scores at either 6 or 8 hours after surgery, we elected to combine these data in the meta-analysis as a one “6 to 8 hour” assessment. In 2 trials, outcome data were reported as median and interquartile range; to facilitate meta-analysis, we requested the mean and standard deviation from the respective corresponding authors.<sup>10,11</sup> Data were extracted from graphs for 2 trials.<sup>12,14</sup>



**Figure 2.** Study flow chart (as per PRISMA guidelines).<sup>7</sup> RCT = randomized controlled trial; RSB = regional scalp block.

### Methodological Quality

Reporting of methodological aspects of the trials was generally incomplete, hampering the assessment of risk of bias within individual studies (Table 2). All included trials were randomized, though the method of sequence generation was not detailed in 6 of the reports. Similarly, the procedure for allocation concealment was only reported for 3 trials. In 6 trials, the neurosurgeon or anesthesiologist was blinded by performing a placebo RSB with saline (including identical concentration of epinephrine to the active arm). In the 2 trials without placebo RSB, the investigator was inherently unblinded; however, as procedures were performed under anesthesia, we considered the subject to be blinded to the intervention. Further, in 1 of the trials without a placebo RSB, the pain score assessment was performed by a blinded assessor. Follow-up was generally good: in 1 study, 5 patients were excluded due to intraoperative complications necessitating continued postoperative sedation,<sup>10</sup> and in a further 2 trials, 6 patients were excluded because of postoperative hematoma and consequent inability to report pain scores. We did not regard any study as exhibiting selective outcome reporting.

### Pain Scores

Meta-analysis was performed separately for pain scores assessed at 1, 2, 4, 6 to 8, 12, and 24 hours postoperatively. The largest effect size was at 1 hour postoperatively with a pooled mean reduction in pain score of 1.61 on the 0 to 10 analog ( $N = 5$  studies; 95% confidence interval [CI],  $-2.06$  to  $-1.15$ ;  $P < 0.001$ ;  $I^2 = 0\%$ ; Fig. 3). There was significant reduction in reported pain scores associated with RSB at 2, 4, and 6 to 8 hours but not at 12 and 24 hours (Table 3, Supplemental Figs. 1–5 in the Appendix). There was no significant heterogeneity in the treatment effect at the 1-hour assessment; however, at subsequent assessments  $I^2$  values ranged from 62% to 81%, indicating significant heterogeneity. The included studies were divided into subgroups depending on whether the RSB was administered preoperatively or postoperatively. Preoperative RSB was significantly effective at 1, 2, and 4 hours after surgery, whereas postoperative RSB showed significant reduction in pain scores at 1, 4, 6 to 8, and 12 hours (Fig. 3 and Supplemental Figs. 1–5). Correspondingly, there was a significant difference between the subgroups at the 6 to 8 hours assessment (Supplemental Fig. 3).

### Analgesia Requirement

Six studies reported sufficient information regarding total parenteral or enteral opioid consumption over the first 24 hours postoperatively to include in a meta-analysis.<sup>10,11,13–16</sup> In the study by Bala et al.<sup>11</sup> none of the patients in the RSB group required opioids (tramadol) within 24 hours, precluding calculation of an MD; to enable this study to be included, a value of 1 mg was entered for mean consumption in the RSB group, and the standard deviation was assumed the same as for the control group. Meta-analysis showed an overall reduction in opioid requirement associated with RSB ( $N = 6$  studies; pooled SMD,  $-0.79$ ; 95% CI,  $-1.55$  to  $-0.03$ ;  $P = 0.04$ ;  $I^2 = 86\%$ ); however, there was significant heterogeneity (Table 3, Fig. 4).

### Adverse Events

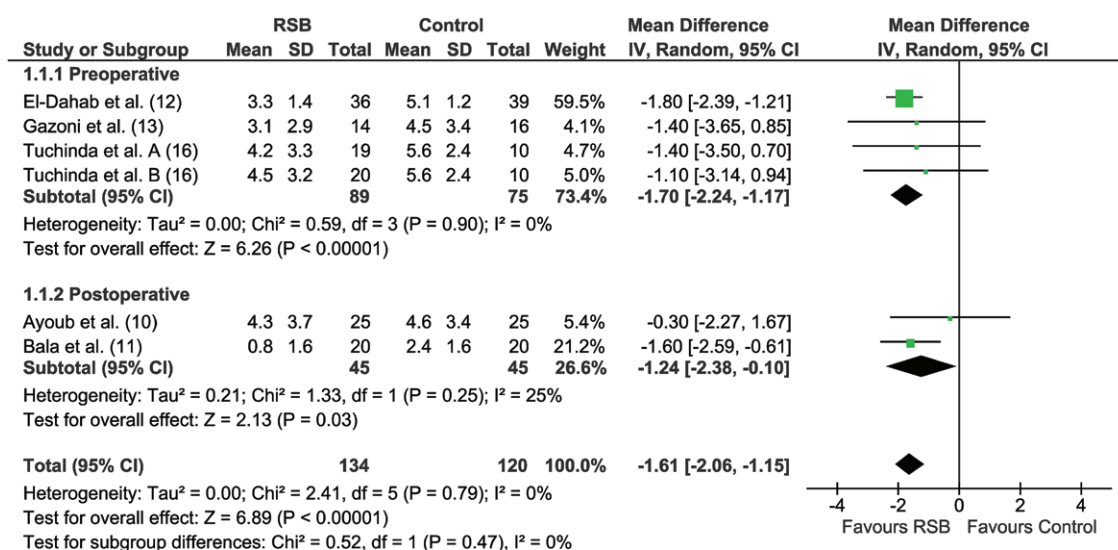
None of the included trials reported any significant difference in the incidence of intraoperative or postoperative complications among study groups, and there were no documented adverse events associated with RSB such as local hematoma, infection, or nerve injury. A pooled 95% CI for the incidence of adverse events was estimated with an inverse-variance weighted fixed-effects model and gave an upper limit of 1.6%.

**Table 2. Risk of Bias Assessment**

	Adequate randomization sequence	Adequate allocation concealment	Investigator blinding	Patient blinding	Assessor blinding	Follow-up completeness (%)	Selective outcome reporting
Ayoub et al. <sup>10</sup>	Unclear	Yes	Yes	Yes	Unclear	100 <sup>a</sup>	No
Bala et al. <sup>11</sup>	Yes	Yes	Yes	Yes	Yes	100	No
El-Dahab et al. <sup>12</sup>	Unclear	Unclear	No	Yes	Yes	94	No
Gazoni et al. <sup>13</sup>	Unclear	Unclear	No	Yes	Unclear	100	No
Hernández Palazón et al. <sup>14</sup>	Unclear	Unclear	Unclear	Yes	Yes	100	No
Nguyen et al. <sup>15</sup>	Unclear	Unclear	Yes	Yes	Yes	100	No
Tuchinda et al. <sup>16</sup>	Unclear	Unclear	Yes	Yes	Unclear	98	No

<sup>a</sup>Five patients excluded after randomization but before administration of regional scalp block/control due to intraoperative complications precluding immediate extubation; all patients receiving intervention followed-up as per protocol.





**Figure 3.** Forest plot summarizing meta-analysis of studies reporting pain scores 1 hour after surgery. CI = confidence interval; RSB = regional scalp block.

### Assessment of Publication Bias

Funnel plots showed the studies with least precision (higher SE) also had the lowest effect size in terms of pain score reduction, the opposite situation to that expected with publication bias<sup>8</sup> (Fig. 5). Correspondingly, Egger test found no significant bias at any of the pain score assessments (all  $P > 0.05$ ).

### DISCUSSION

We systematically reviewed the available evidence to determine whether RSB is clinically effective for postoperative analgesia after supratentorial craniotomy. Seven RCTs meeting the predefined inclusion criteria were identified from the literature search. RSB was performed with a similar technique in all trials, following the procedure described by Pinosky et al.<sup>5</sup> There was no incidence of infection, hematoma, neuropraxia, or other complications attributable to RSB in any of the included trials. Meta-analysis of the pooled trial data demonstrated that RSB is effective at reducing pain after craniotomy. Combining all studies, there was significant reduction in pain scores up to 6 to 8

hours postoperatively; subgroup analysis showed RSB had a longer duration of action when performed postoperatively compared with preoperative injection. There was no evidence of significant publication bias with respect to pain scores at any time point.

### Postcraniotomy Pain

Observational studies have shown that 10% to 25% of patients suffer severe pain after craniotomy, and approximately a further 30% report moderate pain or inadequate analgesia, particularly over the first 24 hours postoperatively.<sup>1,17–19</sup> Furthermore, between 15% and 50% of patients are afflicted by persistent postcraniotomy headache that has significant impact on quality of life, and inadequate analgesia in the acute phase may increase the likelihood of developing chronic symptoms.<sup>17,20,21</sup>

Surveys of health care professionals suggest widespread under-recognition of the frequent incidence of acute postcraniotomy pain, which is reflected in the general absence of standardized pain management protocols.<sup>2,22</sup> Studies have demonstrated that codeine and tramadol significantly

**Table 3. Summary of Meta-Analysis Results**

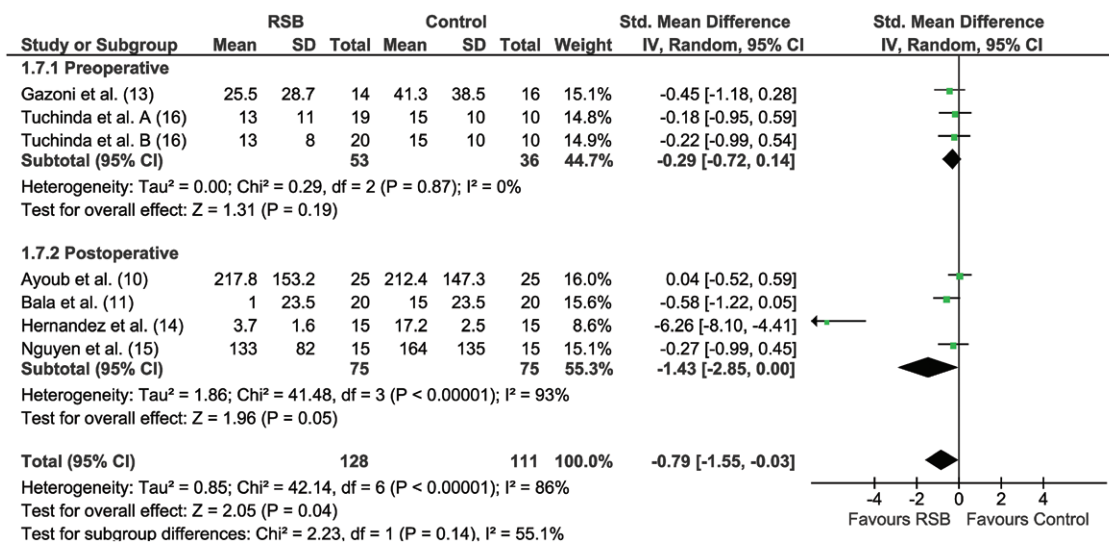
Subgroup	All Studies			Preoperative RSB			Postoperative RSB		
	N <sup>a</sup>	ES <sup>b</sup> (95% CI)	I <sup>2</sup>	N	ES (95% CI)	I <sup>2</sup>	N	ES (95% CI)	I <sup>2</sup>
Pain scores after surgery									
1 h	5 (254)	<b>-1.61 (-2.06 to -1.15)</b>	0	3 (164)	<b>-1.70 (-2.24 to -1.17)</b>	0	2 (90)	<b>-1.24 (-2.38 to -0.10)</b>	25
2 h	6 (284)	<b>-1.34 (-2.26 to -0.42)</b>	80	3 (164)	<b>-1.18 (-2.30 to -0.06)</b>	48	3 (120)	-1.49 (-3.42 to 0.44)	92
4 h	6 (255)	<b>-1.47 (-2.17 to -0.76)</b>	71	2 (105)	<b>-1.11 (-1.67 to -0.55)</b>	0	4 (150)	<b>-1.60 (-2.17 to -0.76)</b>	75
6–8 h	6 (284)	<b>-0.79 (-1.55 to -0.03)</b>	74	2 (134)	-0.10 (-1.01 to 0.82)	35	4 (150)	<b>-1.34 (-2.11 to -0.56)</b>	58
12 h	5 (209)	-0.85 (-1.73 to 0.02)	69	1 (59)	0.08 (-1.16 to 1.31)	0	4 (150)	<b>-1.20 (-2.16 to -0.23)</b>	72
24 h	4 (169)	-0.46 (-1.06 to 0.15)	27	1 (59)	0.27 (-0.93 to 1.48)	0	3 (110)	-0.79 (-1.68 to 0.11)	51
Postoperative opiate requirement	6 (239)	<b>-0.79 (-1.55 to -0.03)</b>	86	2 (89)	-0.29 (-0.72 to 0.14)	0	4 (150)	-1.43 (-2.85 to 0.00)	93

Numbers in bold indicate a significant treatment effect ( $P < 0.05$ ).

CI = confidence interval.

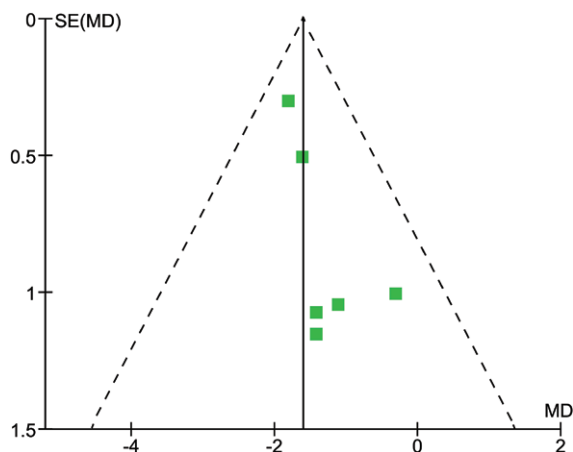
<sup>a</sup>Number of trials pooled (total number of subjects).

<sup>b</sup>Effect size (ES); mean difference for pain score and standardized mean difference for opiate consumption.



**Figure 4.** Forest plot summarizing the meta-analysis opioid consumption in the 24 hours after surgery. CI = confidence interval.

reduce pain compared with placebo but are associated with nausea and vomiting.<sup>23</sup> Nonselective nonsteroidal anti-inflammatory drugs have not been favored because of their inhibition of platelet aggregation and the associated risk of intracranial hematoma. Moreover, neurosurgical patients frequently take high-dose corticosteroids to combat vasogenic brain edema, and nonsteroidal anti-inflammatory drugs are therefore relatively contraindicated due to the additive risk of gastrointestinal bleeding. There has been reluctance to administer systemic strong opioids after craniotomy both because of the perceived lack of need and concern that neurological assessment will be impaired and ventilation depressed causing hypercapnia and an increase in intracranial pressure.<sup>3</sup> In fact, controlled trials of IM and IV morphine demonstrate more effective reduction in pain scores compared with codeine or tramadol without significant respiratory depression, suggesting this risk is somewhat overstated.<sup>24–26</sup> Nonetheless, LA or regional anesthesia that is equally effective or superior to systemic drugs would be preferable.



**Figure 5.** Funnel plot of studies reporting pain scores at 1 hour postoperatively. Solid line indicates the pooled effect size and dashed lines indicate the 95% confidence interval. MD = mean difference; SE (MD) = standard error of the mean difference.

After craniotomy, patients report pain predominantly localized to the incision site and surrounding soft tissues, with a lesser component of generalized diffuse headache, presumably of dural origin. Infiltration of the planned incision with LA and epinephrine is now standard neurosurgical practice, principally to achieve local vasoconstriction and reduce bleeding from the scalp. Studies examining the analgesic efficacy of wound infiltration, either before incision or at the completion of surgery, have shown inconsistent results.<sup>27–30</sup> Moreover, this technique does not block nociceptive afferents to deeper tissues, such as temporalis muscle, which is often divided and reflected as part of a myocutaneous flap, whereas RSB inhibits innervation to both superficial and deep soft tissue layers.

Batoz et al.<sup>27</sup> conducted an RCT ( $N = 52$ ) demonstrating that preincision wound infiltration reduced the incidence of chronic postcraniotomy headache despite having no significant effect on acute perioperative opioid requirements. It is unclear from the available reports whether preoperative RSB similarly reduces the incidence of chronic headache. More generally, although studies in preclinical models have convincingly shown that preemptive analgesia decreases the likelihood of long-term sensitization, the cumulative evidence from patient studies has been largely inconclusive and the clinical application of preemptive analgesia to specifically prevent chronic pain remains controversial.<sup>31</sup>

### Timing of RSB

Separate meta-analysis of the included studies based on timing of RSB showed a differing duration of postoperative analgesia depending on whether administration was before incision or at the time of wound closure. Pooled data from studies of preoperative RSB demonstrated significant reduction in pain scores up to 4 hours postoperatively. By contrast, there was continued significant effect of RSB up to 12 hours when administered at the end of surgery, and the MD in pain scores was significantly different between subgroups at 6 to 8 hours. This finding is unsurprising, and, in practice, the longevity of preoperatively administered RSB will be dependent on the duration of surgery.

For procedures during which the patient is awake intraoperatively to allow electrophysiological mapping and functional testing, RSB performed before surgery is a necessity to minimize discomfort and provide optimal conditions for neurological assessment. Furthermore, even for procedures under general anesthesia, preoperative RSB may have the advantage of blunting hemodynamic responses to noxious stimuli such as skull pinning, skin incision, flap dissection, and craniotomy.<sup>12,13,16</sup> The resulting reduction of intraoperative sedation requirements would facilitate more rapid emergence and lessen cognitive dysfunction after anesthesia. However, the study selection process for the present review specifically excluded trials exclusively reporting autonomic responses as outcomes, and therefore inferences regarding the efficacy of preoperative RSB in this respect cannot be drawn.

### Choice of LA Agent

Four of the included trials used a combination of bupivacaine and epinephrine, 1 used a 1:1 mixture of lidocaine and bupivacaine, and 2 used ropivacaine alone. Both bupivacaine and ropivacaine are long-acting amino-amide LAs with comparable time of onset and duration of action.<sup>32</sup> However, racemic bupivacaine is associated with a higher incidence of cardiac toxicity, a stereospecific side effect that is avoided with ropivacaine or levobupivacaine, both of which are pure S(–)-enantiomers.<sup>32,33</sup> Given the small number of trials in the current meta-analysis, and their methodological heterogeneity, there were insufficient data to perform a valid metaregression or subgroup analysis to indirectly compare bupivacaine and ropivacaine. For the same statistical reasons, it was not possible to interrogate the data to determine whether epinephrine coadministration significantly prolongs the treatment effect of RSB. However, the pharmacology of bupivacaine and ropivacaine is well characterized, and there is unlikely to be a major difference in efficacy for RSB at equivalent dosage.<sup>32,34</sup> Similarly, although levobupivacaine has not been directly evaluated for RSB in an RCT setting, it should also be a suitable choice in clinical practice.<sup>33,35</sup>

### Limitations

All 7 RCTs included in the present review had a relatively small sample size and methodological quality was variably reported, although all were at minimum single blind. Other than at the first (1 hour) pain score assessment, there was significant heterogeneity among the studies, presumably reflecting methodological differences among the included trials, e.g., choice and dose of LA drug and whether or not epinephrine was coadministered. To estimate the effect of RSB on opioid requirements, it was necessary to impute a value for tramadol consumption in the intervention arm of 1 trial<sup>11</sup> as no patient, in fact, required additional analgesia, producing a more conservative estimate of the treatment effect. Notwithstanding this, although the pooled estimate of the difference in opioid consumption was significant, the upper 95% confidence limit was close to zero, and there was significant heterogeneity among the studies, indicating that this finding should be interpreted with caution.

The small sample sizes of the included studies also preclude a precise estimation of the incidence of side

effects or complications of RSB. There are generic risks that apply to any LA infiltration (e.g., intravascular injection and infection) and additional specific risks with RSB such as subarachnoid injection and transient facial palsy.<sup>36</sup> The fact that no complications attributable to RSB were reported in any of the trials included in this review suggests the technique has generally low morbidity, and the upper limit of the estimated 95% CI for the pooled risk was 1.6%. However, this requires validation in larger studies.

Hansen et al.<sup>37</sup> recently published a qualitative systematic review of analgesia interventions for postcraniotomy pain, among them was RSB. However, their search strategy failed to identify 2 published RCTs of RSB that are included in the present review.<sup>12,16</sup> The authors further excluded RCTs of RSB on the basis of non-English language<sup>14</sup> and lack of double blinding<sup>13</sup> and were unable to perform a quantitative meta-analysis of the 2 RCTs meeting their inclusion criteria. In our view, inclusion of single (patient)-blinded RCTs in a meta-analysis is justified, particularly where the primary outcome measure is patient-reported pain scores; translation and inclusion of foreign-language studies is also a good practice to avoid bias.

### Clinical Application of RSB

Although this review has exclusively examined the efficacy of RSB for analgesia after craniotomy, the technique should also be considered for procedures such as cranioplasty, where extensive redisection of the original myocutaneous flap is necessary. Similarly, patients undergoing awake stereotactic surgery (e.g., deep brain stimulator insertion) or radiosurgery may also benefit from RSB to minimize the discomfort of prolonged stereotactic frame application.

### CONCLUSION

Seven RCTs examining the efficacy of RSB for postcraniotomy analgesia met the inclusion criteria. Although the studies varied in methodology and design, there were consistently lower pain scores in the first hour after surgery in the RSB groups across all studies. There were no complications in any of the 170 patients who received RSB. Meta-analysis confirmed RSB was associated with significant reduction in pain for several hours after craniotomy. RSB is a simple and inexpensive technique that can be performed rapidly, safely, and reliably, and the findings of the present study endorse its use for postoperative analgesia in craniotomy procedures. ■

### DISCLOSURES

**Name:** Mathew R Guilfoyle, BSc, MBBCh, MRCS.

**Contribution:** This author helped design the study, conduct the literature search and review, extract the data, perform the analysis, and prepare the manuscript.

**Attestation:** Mathew Guilfoyle approved the final manuscript, reviewed the study original data and analysis, attests to the integrity of the data and analysis reported herein, and is the archival author.

**Name:** Adel Helmy, MA, MB, BChir, PhD, MRCS.

**Contribution:** This author helped conduct the literature review, extract the data, and prepare the manuscript.

**Attestation:** Adel Helmy approved the final manuscript, reviewed the study original data and analysis, and attests to the integrity of the data and analysis reported herein.

**Name:** Derek Duane, MBBCh, FRCA.

**Contribution:** This author helped prepare the manuscript.

**Attestation:** Derek Duane approved the final manuscript.

**Name:** Peter J. A. Hutchinson, BSc, MBBS, PhD, FRCS.

**Contribution:** This author helped prepare the manuscript.

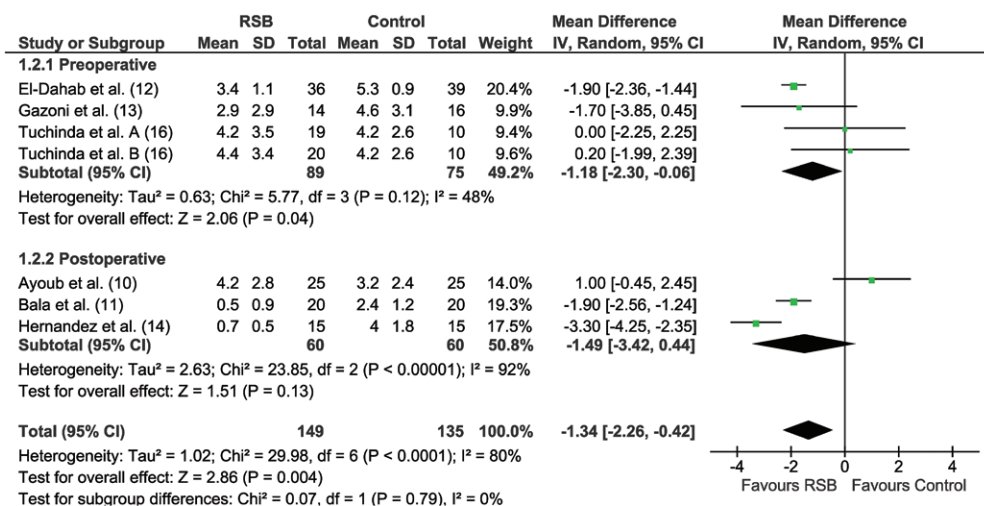
**Attestation:** Peter Hutchinson approved the final manuscript.

**This manuscript was handled by:** Gregory J. Crosby, MD.

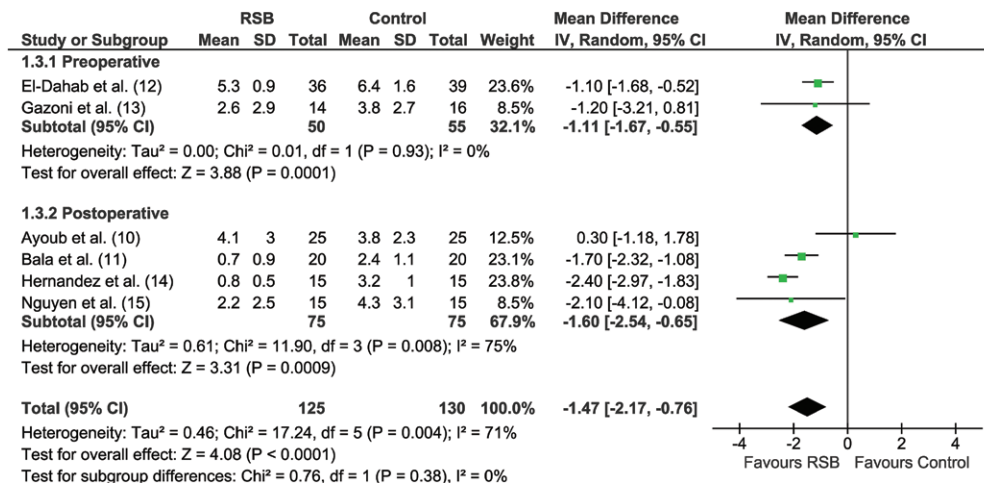
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## APPENDIX

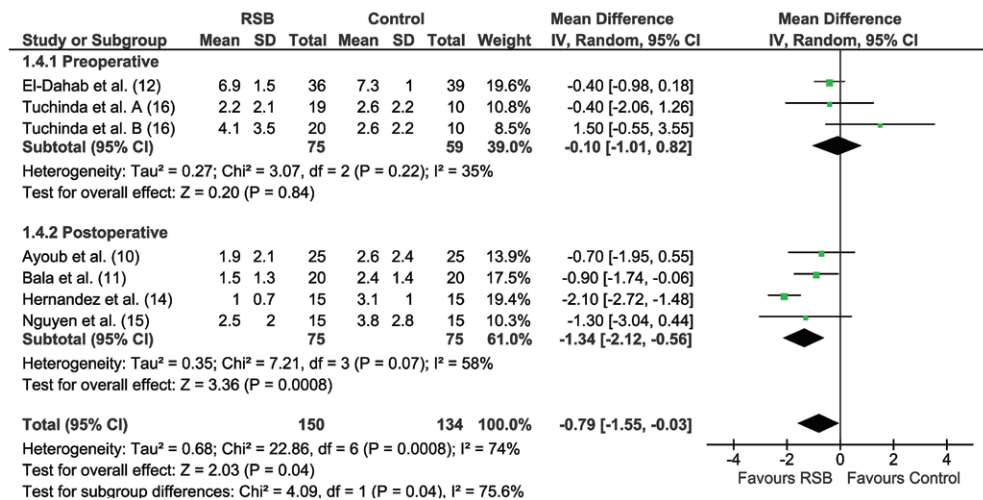


**Supplemental Figure 1.** Forest plot summarizing meta-analysis of studies reporting pain scores at 2 hours after surgery.

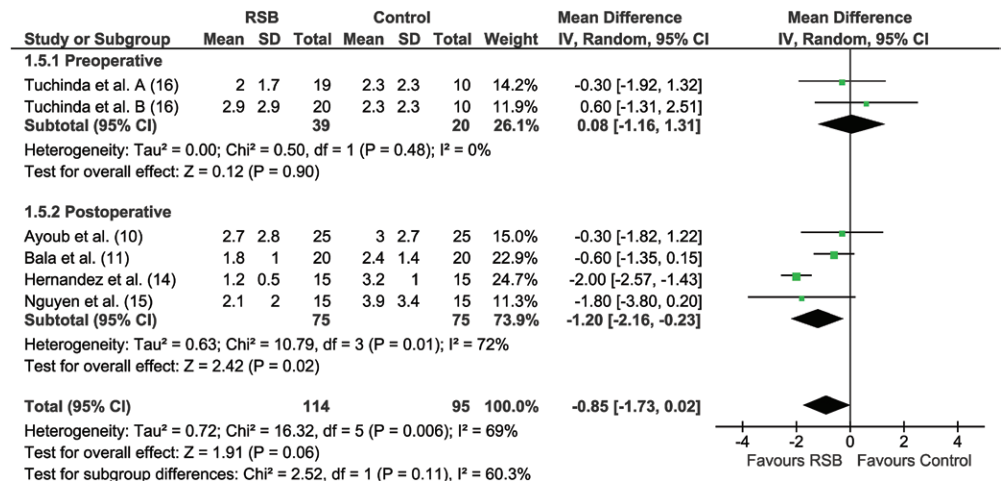


**Supplemental Figure 2.** Forest plot summarizing meta-analysis of studies reporting pain scores at 4 hours after surgery. RSB = regional scalp block; CI = confidence interval.

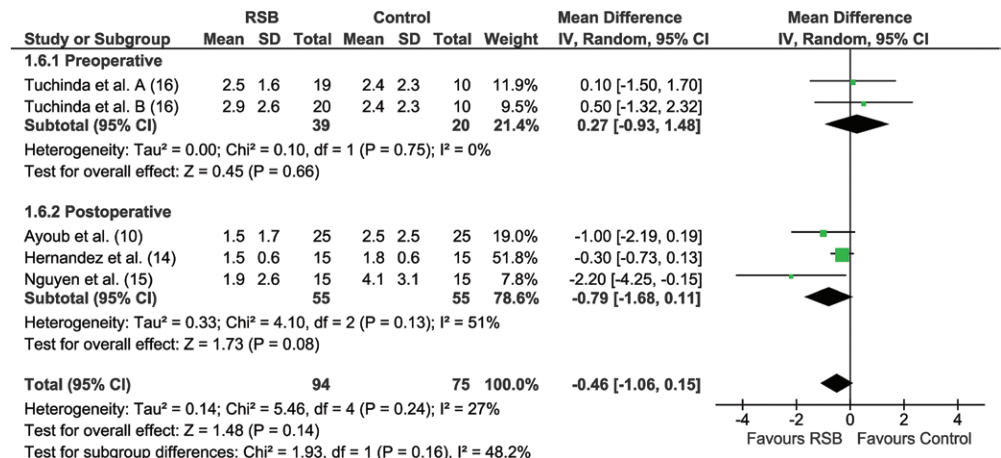




**Supplemental Figure 3.** Forest plot summarizing meta-analysis of studies reporting pain scores at 6 to 8 hours after surgery. RSB = regional scalp block; CI = confidence interval.



**Supplemental Figure 4.** Forest plot summarizing meta-analysis of studies reporting pain scores at 24 hours after surgery. RSB = regional scalp block; CI = confidence interval.



**Supplemental Figure 5.** Forest plot summarizing meta-analysis of studies reporting pain scores at 12 hours after surgery. RSB = regional scalp block; CI = confidence interval.

**Supplemental Table 1. MEDLINE Search Strategy**

1. exp analgesia/ or exp anesthesia, local/ or exp nerve block/ or exp injections, intralesional/ or exp injections, intramuscular/ or exp injections, subcutaneous/ or exp instillation, drug/ or exp Anesthetics, Local/ (local or regional or block\* or infiltrat\* or subcut\* or subderm\* or intraderm\* or subgaleal).ab,ti.
2. (local or regional or block\* or infiltrat\* or subcut\* or subderm\* or intraderm\* or subgaleal).ab,ti.
3. exp Pain/ or exp Pain, Postoperative/ or exp Pain Measurement/ (pain or analgesi\*).ab,ti.
4. exp craniotomy/ (craniotom\* or craniectom\*).ab,ti.
5. or/1-2
6. or/3-4
7. or/5-6
8. and/7-9
9. randomi?ed controlled trial.pt.
10. controlled clinical trial.pt.
11. random\*.tw.
12. placebo.tw.
13. drug therapy.fs.
14. trial.tw.
15. groups.tw.
16. or/11-17
17. exp animals/ not humans.sh.
18. 18 not 19

Specific search for the present study (blue, 1–10) combined with the Cochrane Randomized Controlled Trial Filter (green, 11–20).

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