Comparison of a powered bone marrow biopsy device with a manual system: results of a prospective randomised controlled trial

Christoph Marcus Bucher,1 Thomas Lehmann,1 André Tichelli,1 Alexander Tzankov,2 Stephan Dirnhofer,1 Jakob Passweg,1 Alicia Rovó1

ABSTRACT

The diagnostic and clinical usefulness of a powered bone marrow biopsy device (OnControl®) versus a standard manual device (TRAP Hospital System) was studied. Primary endpoints were biopsy quality and patient pain during the procedure. Fifty patients underwent a total of 60 procedures by three expert operators in a randomised stratified fashion. Baseline demographic and clinical parameters were similar in both groups. The usage of conscious sedation, dosage of lidocaine/pethidin was similar between groups. Biopsy quality was rated ‘sufficient for diagnosis’ in 24/30 in the control group and 25/30 in the powered group (p=0.74). Biopsy cylinder length, procedure time (from skin contact of the biopsy needle to placement of the biopsy cylinder in the formalin container) and patient reported pain during the procedure (T1), 15 min after the procedure (T2) and 3–5 days after the procedure (T3) there were comparable between groups. In the small subgroup of patients that did not receive conscious sedation (n=15; manual 6, powered 9) significantly lower median pain scores were observed with the powered system (median pain score 3 vs 7; p=0.015). Patients were satisfied with either device whether sedation was used (sedation: median 9 for both groups, range 3–10 (manual) and 0–10 (powered)) no sedation (median 8 (manual) vs 9 (powered)). In summary bone marrow biopsies taken with the manual or powered device produce similar technical and clinical results. If no conscious sedation is used, pain during the procedure appears to be lower with the powered system. The use of a powered system seems to be justified in selected patients.

INTRODUCTION

Recent papers have indicated that a powered bone marrow biopsy device (On Control, Vidacare) is superior to manual devices to obtain marrow aspirates and bone marrow biopsies.1–4 An uncontrolled three-centre study1 using a first generation device reported fast insertion into the bone marrow cavity and short aspiration times paired with low insertional and aspirational pain scores in 55 patients. Follow-up studies using a second generation device allows for the extraction of a biopsy core cylinder after aspiration. A randomised study by Berenson1 found that the new device produces significantly larger biopsies, shorter procedure time and reduces intermediate-term pain. Two reports by Swords2 4 found significantly less insertional pain, significantly shortened procedure time, longer marrow biopsies and better operator satisfaction. However, crush artefacts were more abundant with the powered system.

Data from our department,5 a large retrospective study6 and repeated surveys have indicated that the manual procedure is very safe and that the diagnostic yield is generally high. However, in a fraction of patients diagnostic yield is insufficient and could potentially be improved by larger biopsy specimens. The impact of the larger cylinders obtained with the powered device on their diagnostic value has not been addressed.

The primary goal of this study was to determine the clinical relevance of differences of quality of cylinders obtained either with a standard manual device (Hospital TRAPSYSTEM-HS Hospital Service S.p.A., Aprilia Italy 11G×100 mm) or a powered device (OnControlTM, Vidacare, Shavano Park, Texas, USA 11G×103 mm). Further, we wanted to address the hypothesis that the powered system is less painful during and after the intervention, potentially leading to improved patient satisfaction.

METHODS

Trial design

Prospective single centre non-blinded randomised trial.

Patients

The protocol was approved by the ethics committee of Basel and all patients signed informed consent (EKBB 88/11). Both hospitalised patients on the transplant ward and ambulatory patients in the clinic were eligible for inclusion. Recruitment started on May 5th 2011 and was concluded on the 8th of August 2011. Patients could be included and randomised more than once.

End points

Primary endpoint was diagnostic utility of the biopsy. This was judged by a pathologist unaware of the device used. If the pathologist judged that the material was sufficient to make a diagnosis the cylinder was rated 1, in all other cases it was rated 0. Secondary endpoints were cylinder length, number of marrow spaces, and presence of crush or aspiration artefacts. In addition, the quality of the aspirate was rated diagnostic or non-diagnostic. Clinical variables were patient pain during the procedure, 30 min after the procedure and 3–5 days after the procedure. Pain was rated on a visual analogue scale (VAS) from 0–10 with 10 being maximal pain. The patient was also grading his
overall satisfaction on a VAS with the procedure with 10 being maximally satisfied. Procedure time was measured from skin contact of the needle until the biopsy was ejected into the formalin (including aspiration time) by the assisting nurse using a chronometer. To compare the overall pain level during the current procedure with the pain level of previous procedures, patients were asked to indicate the overall pain and satisfaction with previous procedures.

Inclusion/exclusion criteria
Subjects with all of the following characteristics are eligible for study enrolment: age >18 years, ≥one previous bone marrow procedure, INR>1.4, thrombocyte count >10×10⁹/l, informed consent signed. Exclusion Criteria were: cognitive impairment, excessive tissue at anatomical landmarks, body mass index (BMI)> 35 kg/m², allergy to premedication, unable to lay flat in prone position.

Sample size
A preliminary study on 29 cases revealed that cylinders below 11 mm were most likely to be non-diagnostic (25% vs 0%). Medium cylinder length at our centre was 12 mm (SD 6 mm). Therefore, based on the previous reports and these data, we assumed that a median length of 18 mm with a SD of 9 mm should be achievable with the new device. With an α of 0.05 and a power level of 0.9, a sample size of 28 patients per group was needed to reach the primary endpoint. Therefore, we chose to include 30 patients in each arm of the study.

Operators
Three experienced haematologists with >200 conventional biopsies performed. All operators were trained during three procedures with the powered device by training staff of Tinovamed.

Device
The powered device has been described previously. The manual device was a HS Trap system.

Randomisation
A Person unrelated to the procedures did the randomisation. For each operator, differently coloured, labelled and numbered envelopes containing sheets labelled with ‘manual’ or ‘powered’ were put into envelopes in a random fashion prior to initiation of the study. After informed consent was obtained the operator picked the next envelope with his assigned colour.

Analgésia/conscious sedation
Local analgesia was done with 2% subcutaneous lidocaine, conscious analgo-sedation was done according to the departmental standard with intravenous midazolam and intravenous pethidin. Dosages were at the discretion of the operator. Typically 10–20 ml of 2% lidocaine, 20–50 mg pethidin and 2–5 mg midazolam were used. If patients did indicate that sedation was not wanted, only lidocaine was used.

Statistical analysis
Data were written into CRFs by the operators and entered into SPSS v21 by CMB. VAS scores and number of marrow spaces were considered as categorical data and analysed using χ² and Mann-Whitney U test where appropriate. Drug dosages, cylinder length and procedure time were considered continuous data and analysed using students t-test. All p values are two-sided and were considered significant if <0.05.

RESULTS

Patients
Fifty out of fifty-eight screened subjects were randomised (see online supplementary figure S1). The 50 patients were randomised to receive a bone marrow aspirate and biopsy either with a manual device or the powered system. Forty-one patients received one procedure, eight patients received two procedures and one patient received three procedures. Demographic and clinical baseline data are shown in table 1, figure 1.

Biopsy quality
Biopsy quality was rated ‘sufficient for diagnosis’ in 24/30 in the control group and 25/30 in the powered Group (p=0.74). Cylinder length was similar in both groups (figure 2; 14.2 mm (5–37 mm) vs 14.6 mm (6–27 mm), p=0.79). Further parameters of biopsy quality studied were number of marrow spaces, crush artefacts and aspiration artefacts. The median number of marrow spaces was higher in the powered group than in the manual group (n=8 vs 6), but this difference was not statistically significant (p=0.459). By contrast, crush artefacts and aspiration artifacts were slightly more frequent with the powered system than with the manual device (n=17 vs 12 and 14 vs 13), but again this did not reach statistical significance (crush artefacts p=0.301, aspiration artefacts p=1.0). Taken together these data suggest that the quality of biopsy cylinder is comparable using the manual and the powered device, thus our hypothesis that non-diagnostic biopsies could be reduced with the powered system was not confirmed. In both groups, the biopsy could be captured during the first attempt (table 2).

Aspirate quality was equal between groups. No difference in the number of sicca aspirates or in the quality of the smear was observed between groups (data not shown).

Procedure time
The procedure time was measured from skin contact of the biopsy needle to placement of the biopsy cylinder in the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics</th>
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<tr>
<td>Manual</td>
<td>Powered</td>
</tr>
<tr>
<td>N</td>
<td>24</td>
</tr>
<tr>
<td>Procedures</td>
<td>30</td>
</tr>
<tr>
<td>Age (median, range)</td>
<td>56(20–69)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23(18–33)</td>
</tr>
<tr>
<td>Previous procedures (n)</td>
<td>1</td>
</tr>
<tr>
<td>&gt;2</td>
<td>12</td>
</tr>
<tr>
<td>≥6</td>
<td>10</td>
</tr>
<tr>
<td>Diagnosis ALL</td>
<td>6</td>
</tr>
<tr>
<td>AML</td>
<td>5</td>
</tr>
<tr>
<td>CML</td>
<td>4</td>
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<tr>
<td>MDS</td>
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<tr>
<td>MM</td>
<td>3</td>
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<tr>
<td>NHL</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
<tr>
<td>No conscious sedation used</td>
<td>6</td>
</tr>
<tr>
<td>Pain during previous procedure (median, range)</td>
<td>5 (0–10)</td>
</tr>
<tr>
<td>Previous experience with procedure (median, range)</td>
<td>5 (0–10)</td>
</tr>
</tbody>
</table>

ALL, acute lymphoblastic leukemia; AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; MDS, myelodysplastic syndrome; NHL, non-hodkins lymphoma.

formalin container. Although intervention time tended to be shorter with the powered device, there was no significant difference between the groups in procedure time. With the manual system, median time was 180s compared with 150s with the powered system (range 80–480s vs 60–720s; p=0.947).

**Patient pain**
To compare the pain that was experienced by the patients undergoing bone marrow biopsy, the patient was asked to report his/her pain three times: Immediately after the procedure to give an overall score for the whole procedure (T1), 15 min after the procedure, if there was residual pain (T2) and 3–5 days after the procedure to report persistent pain (T3).

In all three time points there was no difference in patient reported median pain between the devices used (pain level manual vs powered T1: 2/10 vs 1/10, T2: 0/10 vs 0/10, T3: 0/10 vs 0/10; p=0.086, p=0.815, p=0.787 respectively). Usage of conscious sedation (24/30 patients and 21/30 patients respectively (p=0.56)) and dosages of lidocaine (10 ml vs 13 ml p=0.24), pethidin (23 mg vs 21 mg, p=0.68) and midazolam (2.5 mg vs 2.6 mg p=0.89) was similar between groups.

At T2 10 Patients reported any pain. Five patients in the manual group had pain levels of 1 (n=3), 2 (n=1) and 3 (n=1). The five patients with T2 pain in the powered device groups

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Results</th>
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<tbody>
<tr>
<td></td>
<td>Manual</td>
</tr>
<tr>
<td>Cylinder diagnostic</td>
<td>24/30</td>
</tr>
<tr>
<td>Cylinder length mm (median, length)</td>
<td>14.2 (5–37 mm)</td>
</tr>
<tr>
<td>Marrow spaces, median, (range)</td>
<td>6 (1–15)</td>
</tr>
<tr>
<td>Fractured cylinder n</td>
<td>12 (40%)</td>
</tr>
<tr>
<td>Aspiration artefacts n</td>
<td>13 (43%)</td>
</tr>
<tr>
<td>Procedure time duration, in seconds median, (range)</td>
<td>180 (80–480)</td>
</tr>
<tr>
<td>Patient pain (median; mean, range)</td>
<td>T1 2: 3.2 (0–10)</td>
</tr>
<tr>
<td>T2 2: 0.28 (0–3)</td>
<td>1: 0.44 (0–5)</td>
</tr>
<tr>
<td>T3 0: 0.86 (0–8)</td>
<td>0: 1 (0–8)</td>
</tr>
<tr>
<td>T1 without conscious sedation</td>
<td>7: 6.3 (3–8)</td>
</tr>
<tr>
<td>Patient satisfaction overall</td>
<td>9 (3–10)</td>
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<tr>
<td>Patient satisfaction without sedation</td>
<td>9 (8–10)</td>
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</table>

**Figure 1** Typical results using the manual and the powered device.

**Figure 2** Patient pain in patients without conscious sedation.
had scores of 1 (n=1), 2 (n=3) and 5 (n=1); p=0.40. At T3
the respective scores for manual and powered were 1 (3; 1), 2
(0; 2), 3 (1; 1), 5 (1; 1), 8(1; 1) p=0.70. Four of these patients
complained about relevant pain (two in each group), including
two patients with post procedural haematoma. Interestingly,
post procedural pain at T2 or T3 did not correlate with the use
of conscious sedation. To control for individual pain perception
patients were asked about pain levels in previous procedures.
The median pain experienced during previous procedures was
similar in both groups (manual median=5, powered=6;
p=0.335). Interestingly these values were significantly higher
than values reported during the trial (manual median=2,
powered median=1).

In the small subgroup of patients that did not receive sedation
(n=15; manual 6, powered 9) significantly lower median pain
scores were observed with the powered system than with the
manual device (median score 3 vs 7 respectively; p=0.015). No
difference was observed in T2 and T3 between devices in this
subgroup.

**Patient satisfaction**

Patients were very satisfied with either device whether sedation
was used (median 9 for both groups, range 3–10 (manual) and
0–10 (powered)) or not (median 8 (manual) vs 9 (powered)).
Patient satisfaction correlated loosely with T1 (R² linear 0.059
and 0.459 for manual and powered, respectively) and procedure
time (R² linear 0.508 and 0.271) without any of these correla-
tions reaching statistical significance.

**Operator satisfaction**

Operator satisfaction was equally high with both devices
(manual: median 8 (6–10), powered 9 (8–10); p=0.213).

**Adverse events**

Adverse events were rare and could not be evaluated statistically.
Two patients in the powered group reported painful haematoma
at T3. One was clinically palpable and had a size of 2×1 cm. The
other was minor. Both resolved. One additional patient in each
group reported persisting pain at T3 (Level manual: 5, OnControl
8; but only while sitting down). One powered insertion needle
broke during the attempt to extract the biopsy specimen.

**DISCUSSION**

This is the first independent prospective randomised trial of a
powered biopsy system capable of aspiration and biopsy through
the same puncture. Our results indicate that the manual system
and the powered device produce comparable results. Our
primary hypothesis, that the powered device would produce sig-
nificantly larger biopsies and therefore help to avoid ‘non-
diagnostic’ biopsies was not met. This is only seemingly in con-
trast with the reports published so far. Diagnostic usefulness was
used as relevant parameter instead of biopsy volume, because if
a minimal size requirement is met, additional marrow spaces
provide no further diagnostic/staging benefit. In this context the
usage of the powered device produced no diagnostic benefit in
our setting. These results are not due to a training effect
because all operators had at least three procedures done before
starting the trial. In addition, no learning curve was observed
during the trial in terms of procedure time or patient pain/satis-
faction levels (data not shown). All operators are very experi-
enced haematologists who did >300 of biopsies with the
manual device before the trial started. Therefore, we can only
speculate whether operators with less experience would have
produced different results. Patient

**Take home messages**

- Manual and powered bone marrow biopsy devices produce
  similar result.

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**Contributors** CMB designed the study, treated patients, analysed data and wrote
the paper, TL treated patients and wrote the paper, AR initiated the project, treated
patients and wrote the paper, ATzankov and SD analysed pathology samples, JP and ATichelli wrote the paper.

Competing interests None.

Patient consent Obtained.

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