

**Clinical trial results:****Magnetic Resonance Imaging of Local Anesthetic Distribution: A Comparison of 5 and 15 milliliters of ropivacaine 0.75% for ultrasound guided interscalene plexus blockade****Summary**

EudraCT number	2013-004219-36
Trial protocol	AT
Global end of trial date	01 April 2015

Results information

Result version number	v1 (current)
This version publication date	16 May 2021
First version publication date	16 May 2021
Summary attachment (see zip file)	Manuscript (REVISED Stundner et al-MRI IS study_Manuscript.docx)

Trial information**Trial identification**

Sponsor protocol code	MR-ISB-1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02175069
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Paracelsus Medizinische Privatuniversität, Universitätsklinik für Anästhesiologie, perioperative Medizin und Intensiv
Sponsor organisation address	Muellner Hauptstrasse 48, Salzburg, Austria, 5020
Public contact	Department of Anesthesia and Intensive Care, Paracelsus Medical University, Muellner Hauptstrasse 48, Paracelsus Medical University, 43 57255, p.gerner1@salk.at
Scientific contact	Department of Anesthesia and Intensive Care, Paracelsus Medical University, Muellner Hauptstrasse 48, Paracelsus Medical University, 43 57255, p.gerner1@salk.at

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 April 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to confirm that the frequency of epidural spread correlates with higher volumes of local anesthetic injection (5ml vs 20ml) after interscalene brachial plexus block.

Protection of trial subjects:

Standard clinical care for routine procedure

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	28
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 30 patients scheduled to undergo shoulder surgery were included. Eligible patients were identified and approached consecutively during their pre-surgical evaluation in the anaesthesia clinic one day prior to surgery, informed about the study, and if they agreed to participate, were asked to provide written consent.

Pre-assignment

Screening details:

Of the 31 patients deemed eligible for participation, thirty (96.8%) agreed to participate.

Period 1

Period 1 title	Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind ^[1]
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

On the day of surgery, an unblinded anaesthesia nurse not otherwise involved in the study prepared the study medication according to the randomisation result in the envelope. All blocks were performed in the MRI scanner anteroom, by a blinded single practitioner (GF) with many years of experience in regional anaesthesia.

Arms

Are arms mutually exclusive?	Yes
Arm title	Low Volume Group

Arm description:

Patients received 5 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.0125 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Arm type	Experimental
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

5 ml ropivacaine 0.75%

Investigational medicinal product name	Gadopentetat-Dimeglumine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Perineural use

Dosage and administration details:

0.0125mmol

Arm title	High Volume Group
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Arm description:

Patients received 20 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.05 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Arm type	Experimental
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Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use
Dosage and administration details: 20 ml ropivacaine 0.75%	
Investigational medicinal product name	Gadopentetat-Dimeglumine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Perineural use
Dosage and administration details: 0.05mmol	

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The block provider (anesthesiologist) was not blinded.

Number of subjects in period 1	Low Volume Group	High Volume Group
Started	15	15
Completed	15	15

Period 2

Period 2 title	Analysis
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind ^[2]
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Low Volume Group

Arm description:

Patients received 5 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.0125 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Arm type	Experimental
Investigational medicinal product name	Gadopentetat-Dimeglumine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Perineural use

Dosage and administration details:

0.0125mmol

Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use
Dosage and administration details: 5 ml ropivacaine 0.75%	
Arm title	High Volume Group

Arm description:

Patients received 20 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.05 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Arm type	Experimental
Investigational medicinal product name	Gadopentetat-Dimeglumine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Perineural use

Dosage and administration details:
0.05mmol

Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:
20 ml ropivacaine 0.75%

Notes:

[2] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The block provider (anesthesiologist) was not blinded.

Number of subjects in period 2	Low Volume Group	High Volume Group
Started	15	15
Completed	15	15

Baseline characteristics

Reporting groups

Reporting group title	Low Volume Group
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Reporting group description:

Patients received 5 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.0125 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Reporting group title	High Volume Group
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Reporting group description:

Patients received 20 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.05 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Reporting group values	Low Volume Group	High Volume Group	Total
Number of subjects	15	15	30
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	50	55	
standard deviation	± 17	± 14	-
Gender categorical			
Units: Subjects			
Female	6	9	15
Male	9	6	15
procedure type			
Units: Subjects			
Arthroscopic	10	13	23
Open	5	2	7
BMI			
Units: kg/m ²			
arithmetic mean	26.3	26.7	
standard deviation	± 5.4	± 4.7	-
Craniocaudal distance			
Craniocaudal distance			
Units: mm			
arithmetic mean	115.6	115.3	
standard deviation	± 10.1	± 10.3	-
Transaxial distance			

Units: mm			
arithmetic mean	127.1	126.2	
standard deviation	± 18.1	± 16.3	-
Neck coefficient			
Units: none			
arithmetic mean	0.92	0.92	
standard deviation	± 0.12	± 0.12	-

End points

End points reporting groups

Reporting group title	Low Volume Group
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Reporting group description:

Patients received 5 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.0125 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Reporting group title	High Volume Group
-----------------------	-------------------

Reporting group description:

Patients received 20 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.05 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Reporting group title	Low Volume Group
-----------------------	------------------

Reporting group description:

Patients received 5 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.0125 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Reporting group title	High Volume Group
-----------------------	-------------------

Reporting group description:

Patients received 20 ml of ropivacaine 0.75% (Naropin®; AstraZeneca Austria GmbH, Vienna, Austria) mixed with 0.05 mmol of the contrast dye, gadopentetate-dimeglumine (Magnevist® 0.5 mmol ml⁻¹; Bayer Vital GmbH, Leverkusen, Germany).

Primary: epidural spread

End point title	epidural spread
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End point description:

End point type	Primary
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End point timeframe:

during MRI

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no epidural spread	13	13		
epidural spread	2	2		

Statistical analyses

Statistical analysis title	chisq
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Comparison groups	High Volume Group v Low Volume Group
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Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Chi-squared

Secondary: spread around intervertebral foramen

End point title	spread around intervertebral foramen
End point description:	
End point type	Secondary
End point timeframe: during MRI	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no spread	15	11		
spread	0	4		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.032
Method	Chi-squared

Secondary: spread around phrenic nerve

End point title	spread around phrenic nerve
End point description:	
End point type	Secondary
End point timeframe: during MRI	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no spread	13	1		
spread	2	14		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Chi-squared

Secondary: intramuscular spread

End point title	intramuscular spread
End point description:	
End point type	Secondary
End point timeframe:	
during MRI	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
spread	6	15		
no spread	9	0		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Chi-squared

Secondary: time to start of pca

End point title	time to start of pca
End point description:	
End point type	Secondary
End point timeframe: during study	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: minutes				
median (standard deviation)	498 (± 245)	755 (± 230)		

Statistical analyses

Statistical analysis title	mannw
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.013
Method	Wilcoxon (Mann-Whitney)

Secondary: PCA ropivacaine consumption

End point title	PCA ropivacaine consumption
End point description:	
End point type	Secondary
End point timeframe: during study	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: milliliters				
median (standard deviation)	142 (± 42)	118 (± 117)		

Statistical analyses

Statistical analysis title	mannw
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.71
Method	Wilcoxon (Mann-Whitney)

Secondary: diclofenac consumption

End point title	diclofenac consumption
End point description:	
End point type	Secondary
End point timeframe:	
during study	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no diclofenac	9	12		
diclofenac	6	3		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.23
Method	Chi-squared

Secondary: paracetamol consumption

End point title	paracetamol consumption
End point description:	
End point type	Secondary
End point timeframe: during study	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no paracetamol	9	11		
paracetamol	6	4		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.44
Method	Chi-squared

Secondary: piritramid consumption

End point title	piritramid consumption
End point description:	
End point type	Secondary
End point timeframe: during study	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
no piritramid	12	14		
piritramid	3	1		

Statistical analyses

Statistical analysis title	chisq
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.28
Method	Chi-squared

Secondary: pain at rest

End point title	pain at rest
End point description:	
End point type	Secondary
End point timeframe:	
postop	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: VAS				
arithmetic mean (standard deviation)	0.47 (± 1.36)	0.43 (± 1.36)		

Statistical analyses

Statistical analysis title	ANOVA
Comparison groups	Low Volume Group v High Volume Group

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.98
Method	ANOVA

Secondary: pain with movement

End point title	pain with movement
End point description:	
End point type	Secondary
End point timeframe: postop	

End point values	Low Volume Group	High Volume Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: vas				
arithmetic mean (standard deviation)	1.07 (\pm 2.09)	0.50 (\pm 1.87)		

Statistical analyses

Statistical analysis title	anova
Comparison groups	Low Volume Group v High Volume Group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.89
Method	ANOVA

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Entire Study Period

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no minor adverse events.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/2686513>