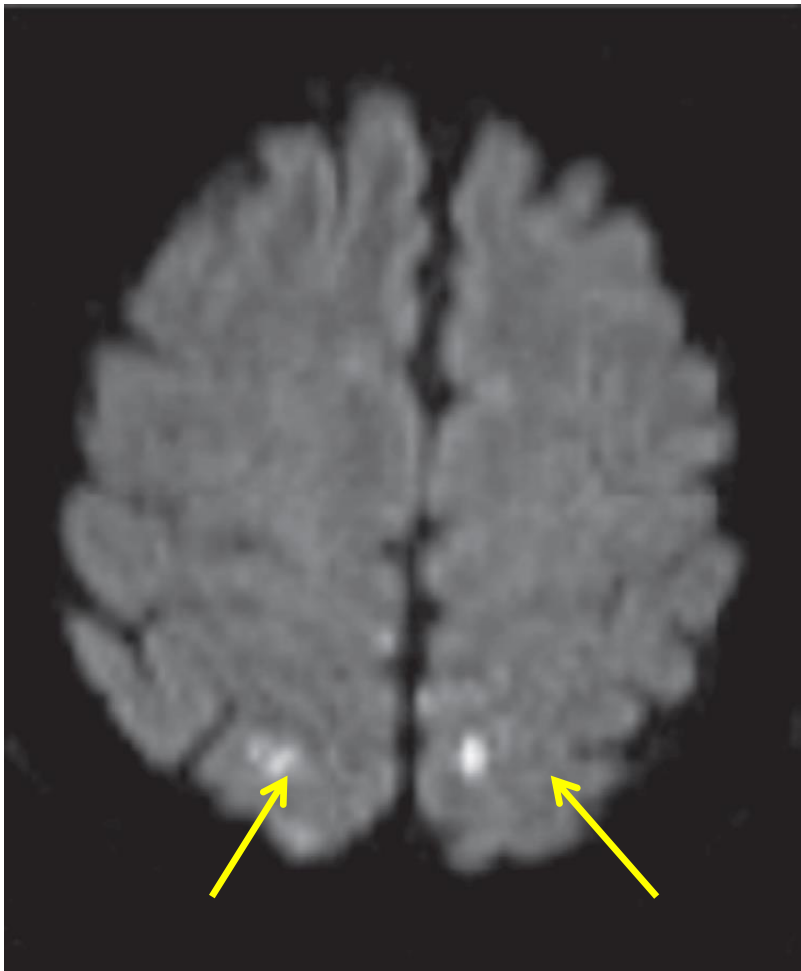


A novel Heparin Infusion Regimen for maintenance of stable ACT values during EP procedures

Neurological events in EP

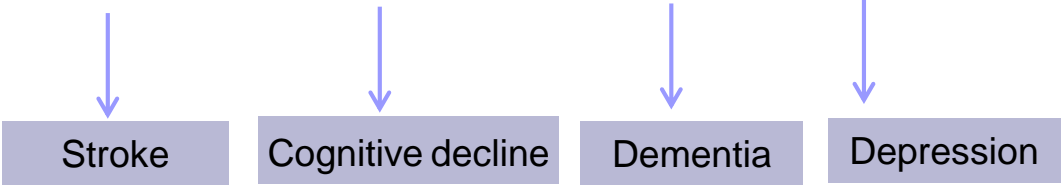
- Current guidelines recommend administration of heparin to ACT > 300 secs
- Risk of stroke quoted at 0.25 – 0.5 %
- Silent Cerebral Ischaemia (SCI) as high as 40 -50 %
- *Gaita et al, Circulation 2010*
- *Haeusler et al, J Card Electr 2013*



*Di Biase et al, Heart Rhythm
May 2014*



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ERACE Study (Verma et al, 2013)

- Low incidence of SCI when multifactorial procedural changes applied (1.7 %, 1/60 pt)
- Amongst these, maintenance of ACT >350s
- **However:**
 1. large SD of mean ACT (405+-116) and first ACT (368 +-192);
 2. Exclusion of patients on NOACs;
 3. No control group



Current practice at Oxford University Hospitals

- Initial heparin bolus (100u/kg if on Warfarin; 150 u/kg if on NOAC) followed by an infusion fixed at 1000 u/hr via irrigation catheter; if ACT below target, intermittent top-up boluses.
- No data on efficacy. Subjective impression is that top-up boluses are frequent.
- To avoid a see-saw effect ,optimizing the infusion regimen would be desirable.



Questions

- How many times do we achieve/maintain our target ACT with standard practice ? How many times do we have to top-up ?
- Can we improve our success rate by using an optimal post-initial bolus heparin infusion?
- Once a satisfactory initial target ACT is achieved, how much do subsequent ACTs vary from baseline? What is the % of variation when we compare a standard heparin bolus technique with an optimized infusion ?

What Heparin infusion ?

1. Based on patient's weight .

Group from South Korea, JACC June 2016. 332 patients needed to show modest improvement over intermittent bolus technique. (64% vs 58%). Convolute administration nomogram. **We did not using this method**

2. Based on initial effective heparin dose .

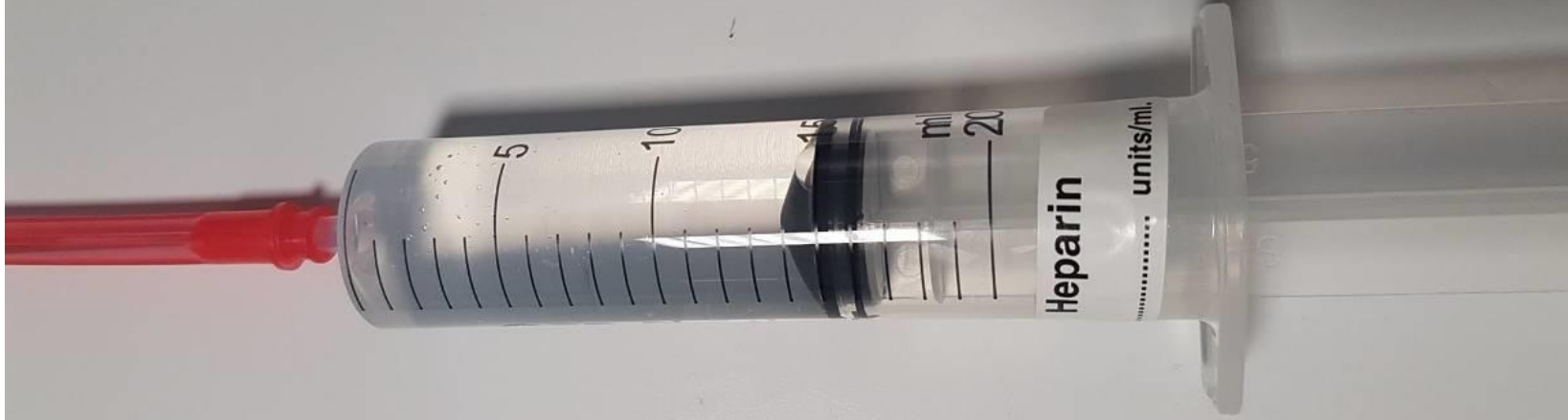
Washington Uni St Louis, USA, approach. Studies on volunteers led to linear regression equation : $T_{1/2} \text{ heparin (min)} = \text{initial bolus dose (U/kg)} \times 0.3 + 33$

Modified in practice so to administer 1/3 of **initial effective bolus** dose in hourly terms,,i.e. if bolus 15000U, infusion to follow at 5000U/hr.

Used on cardiac bypass cases for many years.

Subject of this project.

15000 U





Methods

- 84 patients ; 51 hep infusion (*Infusion group*) v 33 standard management (*Control group*).
- 1 excluded (bolus overshoot), some other missing data

RESULTS

- No difference in age (63 v 60 y $p=0.14$), weight (88 v 89 kg $p=0.8$).
- No difference in 1st heparin bolus dose (10787 v 10980U $p=0.81$), 1st target ACT (346 v 347 $p=0.9$), mean number of ACT samples per patient (4.0 v 4.7 $p=0.2$)

Timing of 1st ACT measurement

- Standard practice at Oxford University Hospitals is to wait for 20-30 mins before measuring the first ACT
- In total, 21 out of 84 initial ACTs were unsatisfactory (25%) (equally distributed, 8 of 33 bolus group, 13 of 51 infusion, $p = 0.54$)
- In the first 30 mins, up to 30% pts may be inadequately anticoagulated. Earlier 1st ACT measurement recommended

Results

Counting from 1st effective ACT (included), overall **337** samples. **Target ACT** achieved :

**180/194 (heparin infusion) v
97/143 (standard)**

$P < 0.001, \chi^2$

Good ACTs **92.8%** (infusion)v **70.7 %** (standard)

Boluses needed per patient :

0.3 (infusion) v **1.4** (standard), $P < 0.001$

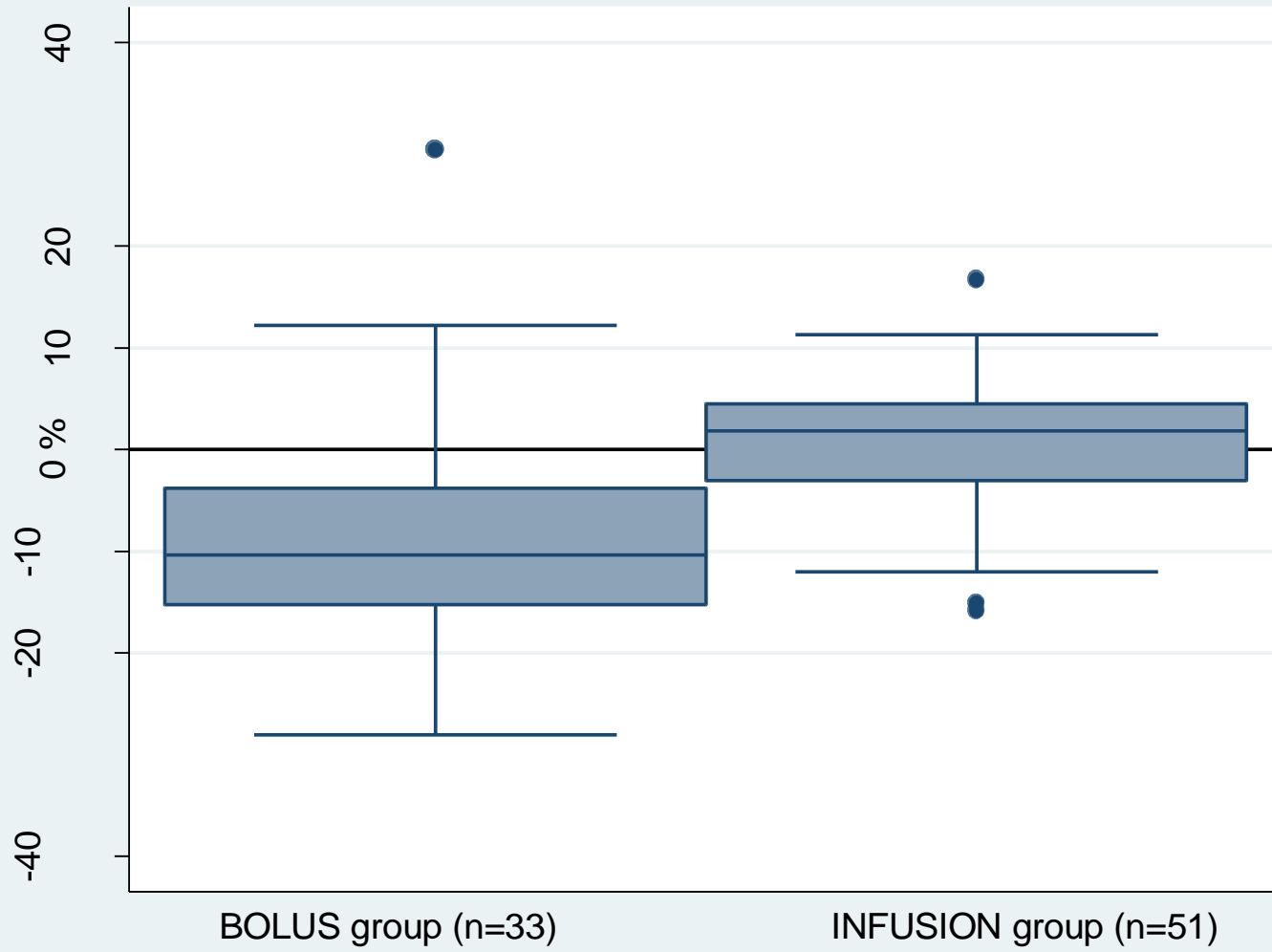
How stable were subsequent ACTs ?

- Mean +SD+ 95% Confidence intervals of all ACTs in both groups (from 1st good ACT included)

Bolus standard : 341 (46), ~~333 - 348~~
Heparin Infusion : 357 (27), **353 - 361** P <0.001

- Mean % variation from initial target ACT

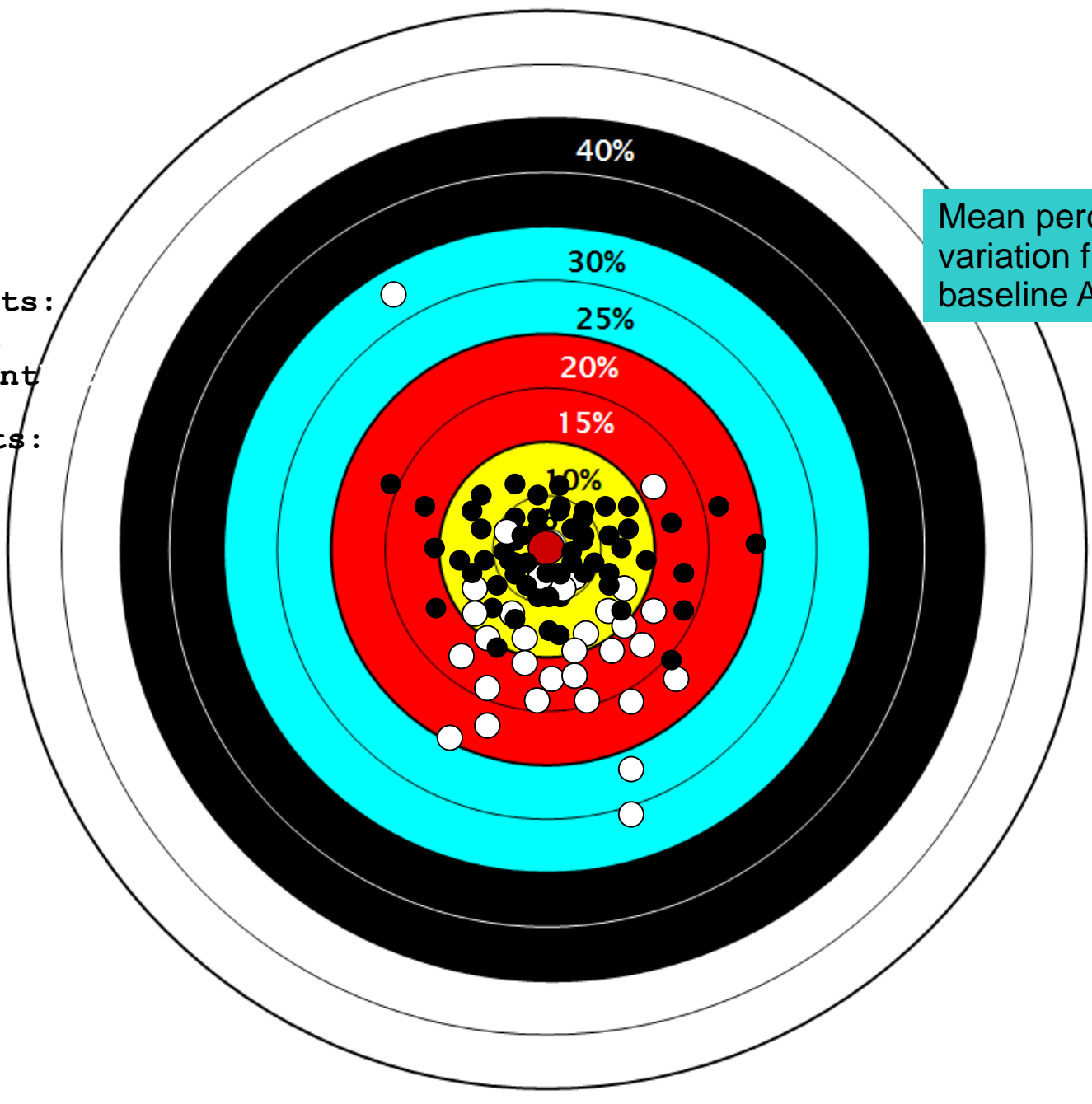
Bolus standard : **- 9.2%** (11.7), -13.4 / - 5.0
Infusion: **0.68 %** (6.2), -1.0 / 2.4 P < 0.001





White dots:
Standard
Management

Black dots:
Heparin
infusion



Mean percentage
variation from target
baseline ACT

Conclusion

- Heparin infused at 1/3 of initial adequate bolus dose (in u/hr) is more effective than standard management at maintaining target ACT
- It produces extremely stable ACT values and avoids fluctuations in anticoagulation
- It requires elementary calculations and very simple set-up and it is not associated with side-effects or complications other than standard
- It could help decreasing the incidence of silent cerebral ischemia.



Thank you



What now ?

- Implementation in our Department
- Prospective randomized study
- Assessment of response to NOACs if stopped / continued
- Impact on Silent Cerebral Ischaemia
- Any other ideas?

Anticoagulation stopped or not

Standard Bolus, n 18

ANTICOAG	STOP	CONT
RIVAROX	3	2
DABIGATRAN	1	1
APIXABAN	1	3
WARFARIN	0	7
NOTHING		

Heparin infusion, n 35

ANTICOAG	STOP	CONT
RIVAROX	8	1
DABIGATRAN	4	1
APIXABAN	11	1
WARFARIN	1	7
NOTHING		1

Bolus/sample ratio

Control group, anticoagulation NOT stopped

■ Rivaroxaban 2 / 11

■ Apixaban 7 / 16

■ Dobigatran 3 / 8

■ Warfarin 9 / 32

21 / 67 (32/109 total in the group)

Mechanism of action

- Rivaroxaban Anti Xa
- Apixaban Anti Xa
- Dabigatran Anti IIa (Antithrombin)

Scatter graphs

