

USE OF ACCELEROMETER DATA TO
EVALUATE PHYSICAL ACTIVITY AS
A SURROGATE ENDPOINT IN HEART
FAILURE CLINICAL TRIALS

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BACKGROUND

- Patient activity levels are of increasing clinical interest to heart failure specialists
- Recent technology developments allow for easy collection of activity data from accelerometers in watches, phones, etc.
- As heart failure treatment has improved over time, clinical trials that use mortality as a primary endpoint are no longer pragmatically or financially feasible

GOALS

1. Can accelerometer data from implantable devices be summarized as a meaningful derived clinical variable?
2. Is this derived variable correlated with standard HF clinical outcomes?
3. Can the derived variable be used as a surrogate endpoint in HF clinical trials?

GOAL #1

Can accelerometer data from implantable devices be summarized as a meaningful derived clinical variable?

ACCELEROMETER DATA IN IMPLANTABLE DEVICES

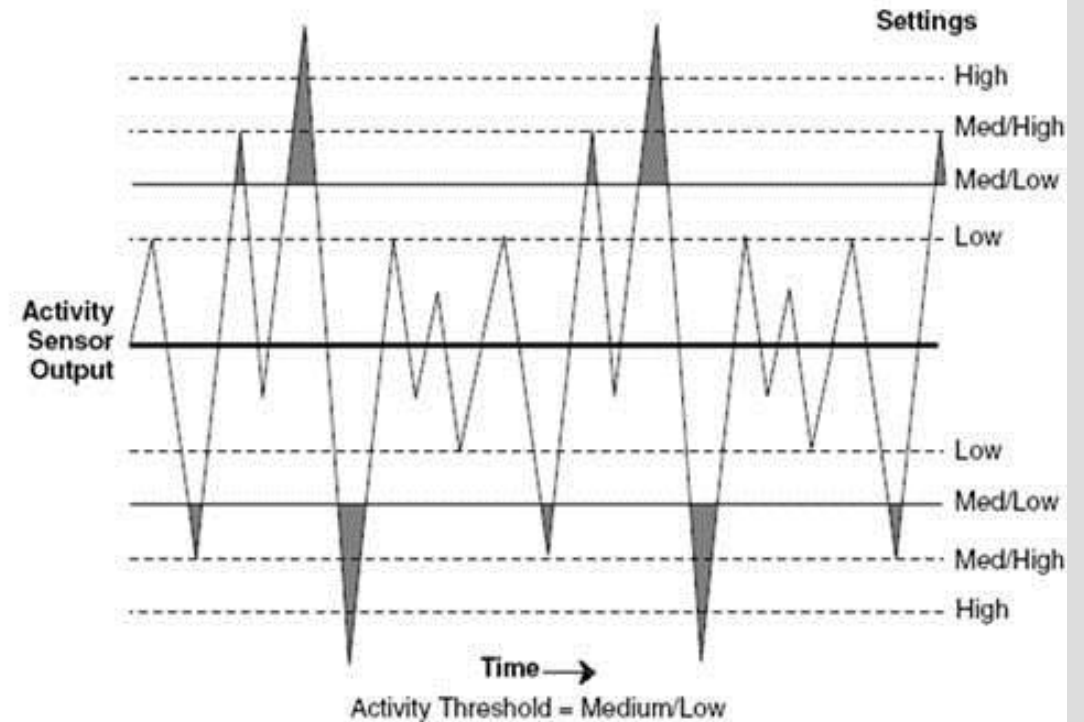
Activity is measured by accelerometer in a pacemaker or insertable cardiac monitor.

In a given minute, implantable devices use a single-axis accelerometer to convert raw units to a counter. If the counter is above a fixed pre-determined threshold, the minute is called “active”.

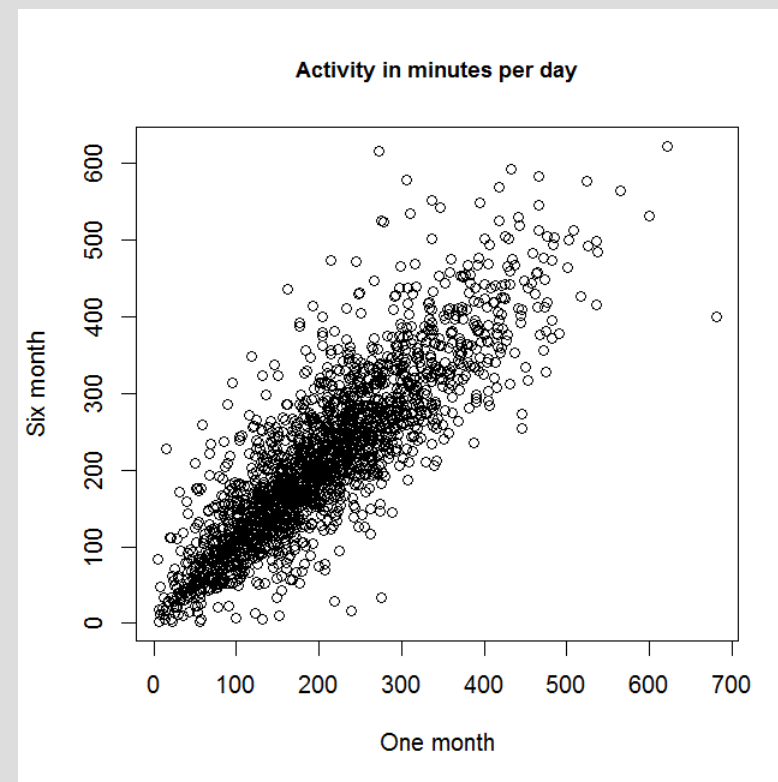
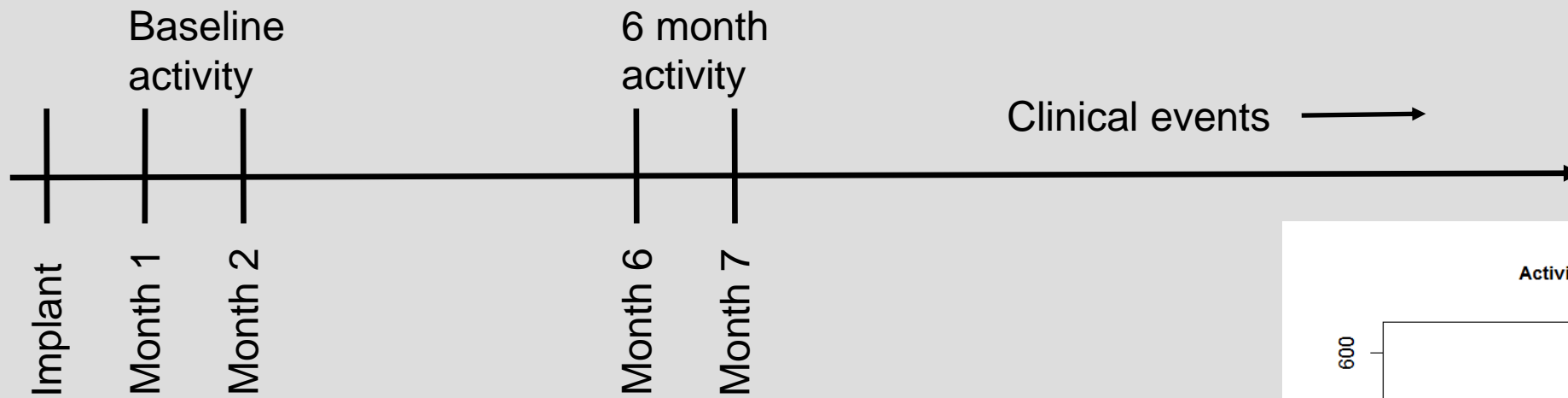
The derived activity variable is the average activity in a month = $\sum_{i=1}^{30} \sum_{j=1}^{1440} x_{ij} / 30$ where $x_{ij} = I(\text{active minute})$.

Rate response programming impacts the counter resulting in differing activity levels

Accelerometer Signal: Threshold



MEASURING CHANGES IN ACTIVITY



GOAL #2

Is this derived variable correlated with standard HF clinical outcomes?

PATIENT DATA

Patients: 2249 patients from the RAFT and REVERSE randomized studies of CRT (cardiac resynchronization therapy)

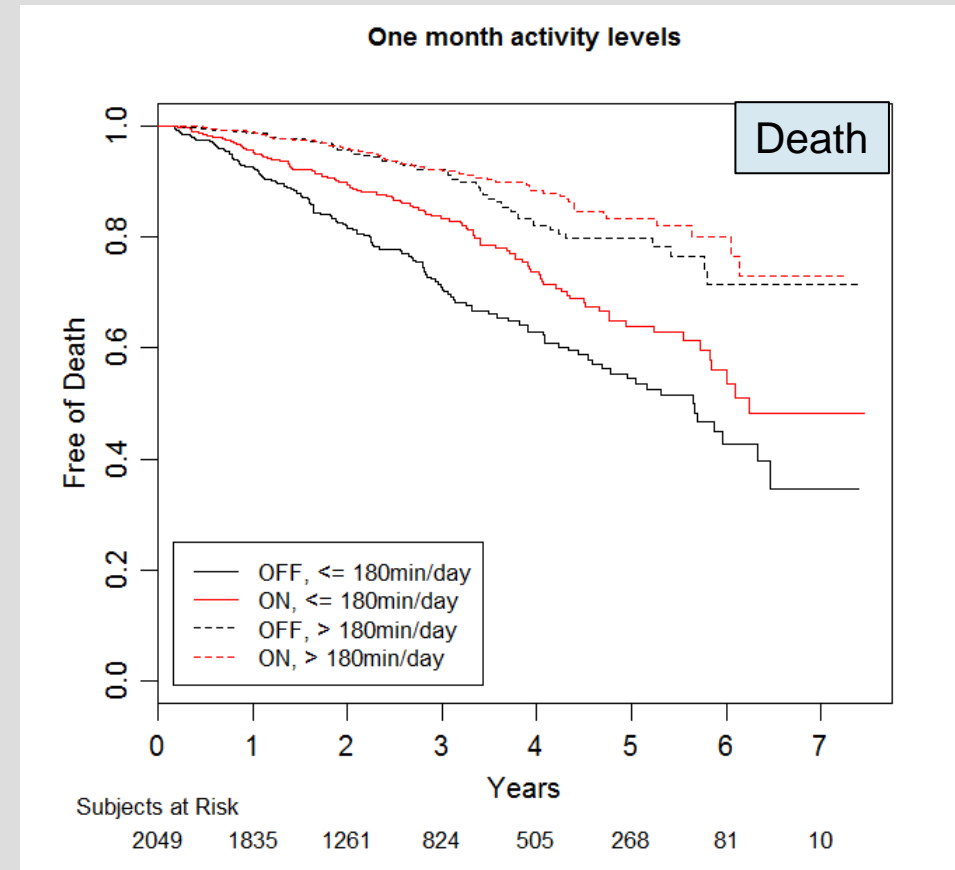
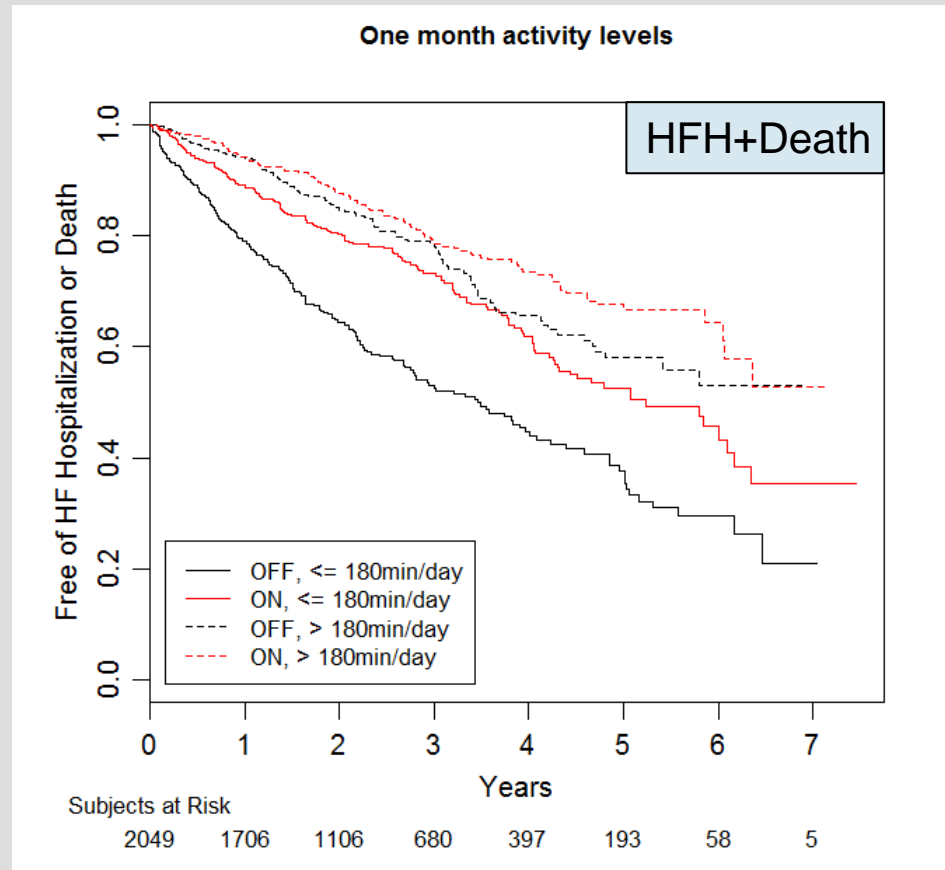
Age: 65 ± 10 years , 82% men, LVEF: $23 \pm 6\%$,
NYHA I 4%, NYHA II 81%, NYHA III 15%

Follow-up: 35 ± 20 months

HF outcomes: Combination HFH/mortality, mortality, and NYHA class at 12 months

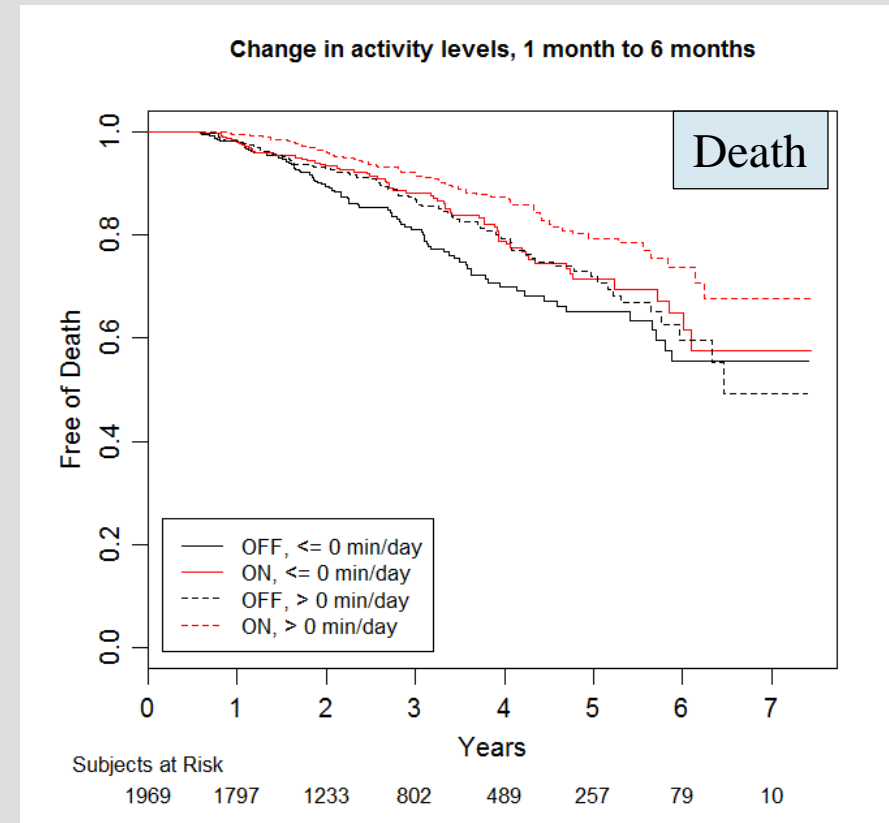
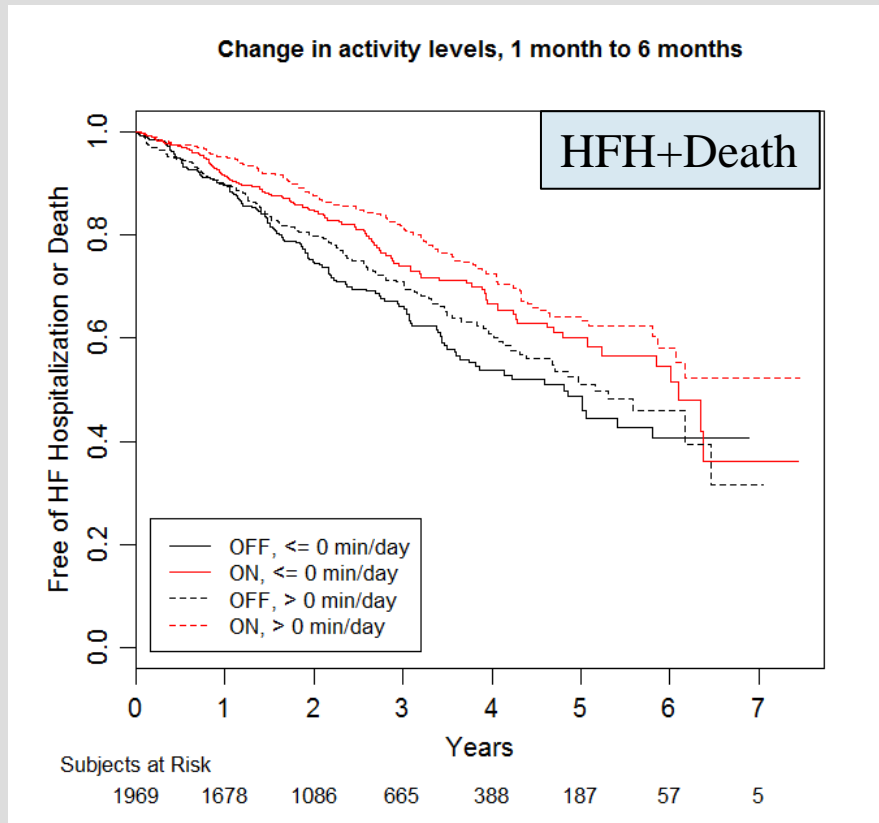
During the follow up 404 pts died and 445 pts had HF hospitalization

CORRELATION OF BASELINE PA WITH LONG TERM HF OUTCOMES?



Analysis adjusted for baseline variables		Death or HF hospitalization	Death	Improvement in NYHA class at 12 months
Activity variable	N	HR (95% CI); P-value	HR (95% CI); P-value	OR (95% CI); P-value
One month PA	2042	0.96 (0.94–0.97); P<0.0001	0.94 (0.92–0.95); P<0.0001	1.02 (1.01-1.04); P=0.004

CORRELATION OF INCREASE IN PA 1-6 MONTHS WITH LONG TERM HF OUTCOMES?



Adjusted for baseline variables

Death or HF hospitalization

Death

Improvement in NYHA class at 12 months

Activity variable

N

HR (95% CI); P-value

HR (95% CI); P-value

OR (95% CI); P-value

Δ PA from 1 to 6 months

1963

0.99 (0.97–1.01); P=0.47

0.97 (0.94–1.00); P=0.04

1.03 (1.00-1.06); P=0.03

OTHER REFERENCES

- Conraads VM et al, Physical Activity Measured With Implanted Devices Predicts Patient Outcome in Chronic Heart Failure, *Circulation: HF*, 2014.
- Snipelisky D et al, Accelerometer-Measured Daily Activity in Heart Failure with Preserved Ejection Fraction, *Circulation: HF*, 2017.
- Jamé S et al, Predictive value of device-derived activity level for short-term outcomes in MADIT-CRT, *Heart Rhythm*, 2017

GOAL #3

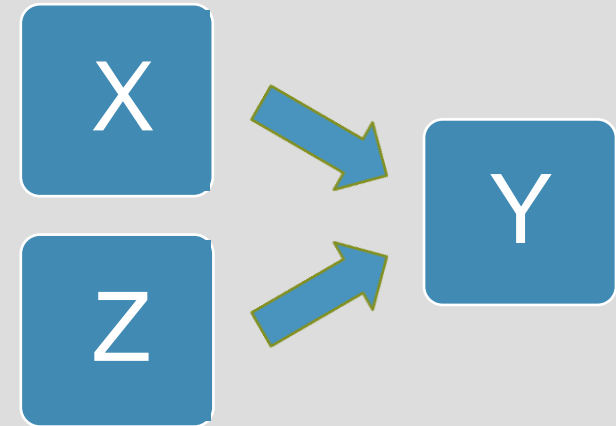
Can the derived variable be used as a surrogate endpoint in HF clinical trials?

CRITERIA FOR A SURROGATE ENDPOINT

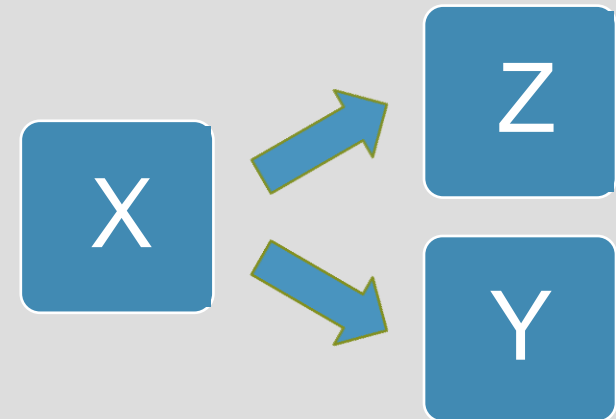
THIS:





NOT THIS:



NOT THIS:



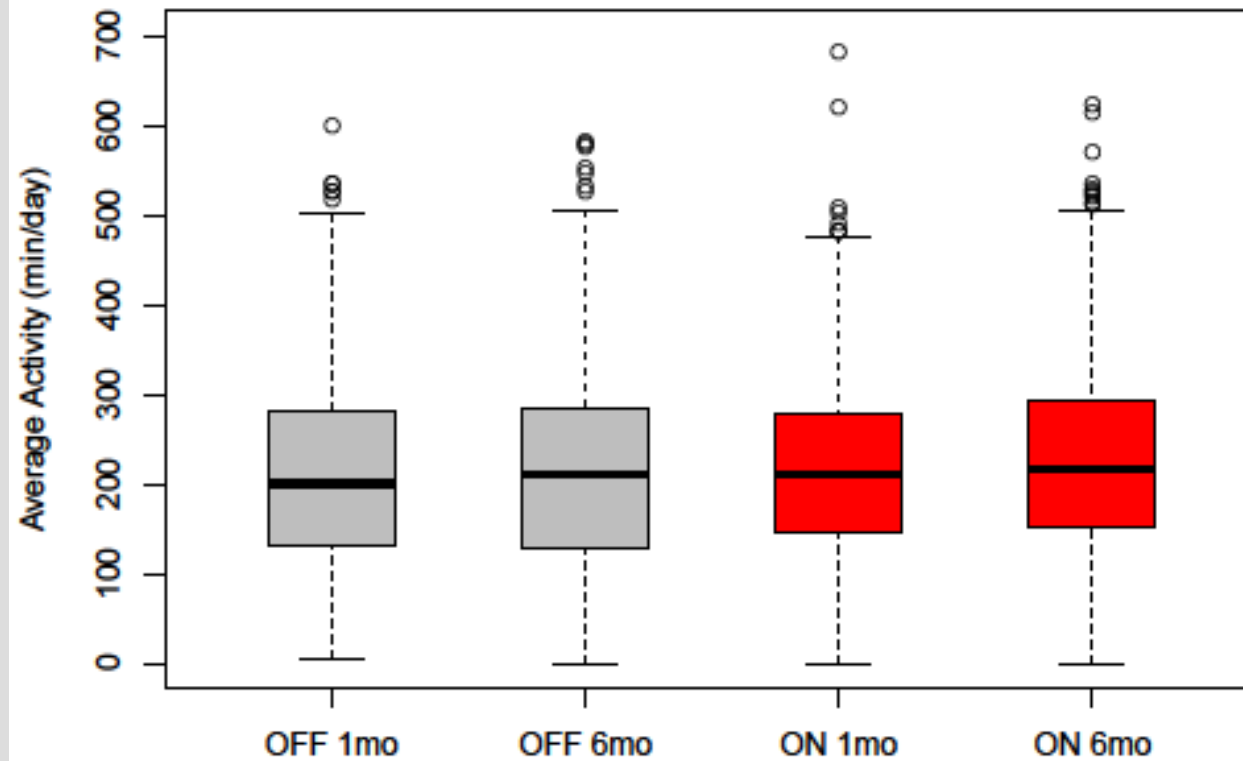
CRITERIA FOR A SURROGATE ENDPOINT

1. Does the primary endpoint Y differ by randomization group X ? 
2. Is the surrogate endpoint Z associated with the primary endpoint Y ? 
3. Does the surrogate endpoint Z differ by randomization group X ?




Prentice criterion: $f(Y|Z) \perp X$

ACTIVITY LEVELS BY RANDOMIZATION

Devices with Rate Response Programming Settings Available N=1262



CRITERIA FOR A SURROGATE ENDPOINT

1. Does the primary endpoint Y differ by randomization group X?

2. Is the surrogate endpoint Z associated with the primary endpoint Y?

3. Does the surrogate endpoint Z differ by randomization group X?


CONCLUSIONS

- Goal #1 met. We can derive meaningful clinical variables from accelerometers in implantable devices
- Goal #2 met. The derived variables are associated with standard clinical outcomes in heart failure.
- Goal #3 not met. Further investigations underway.

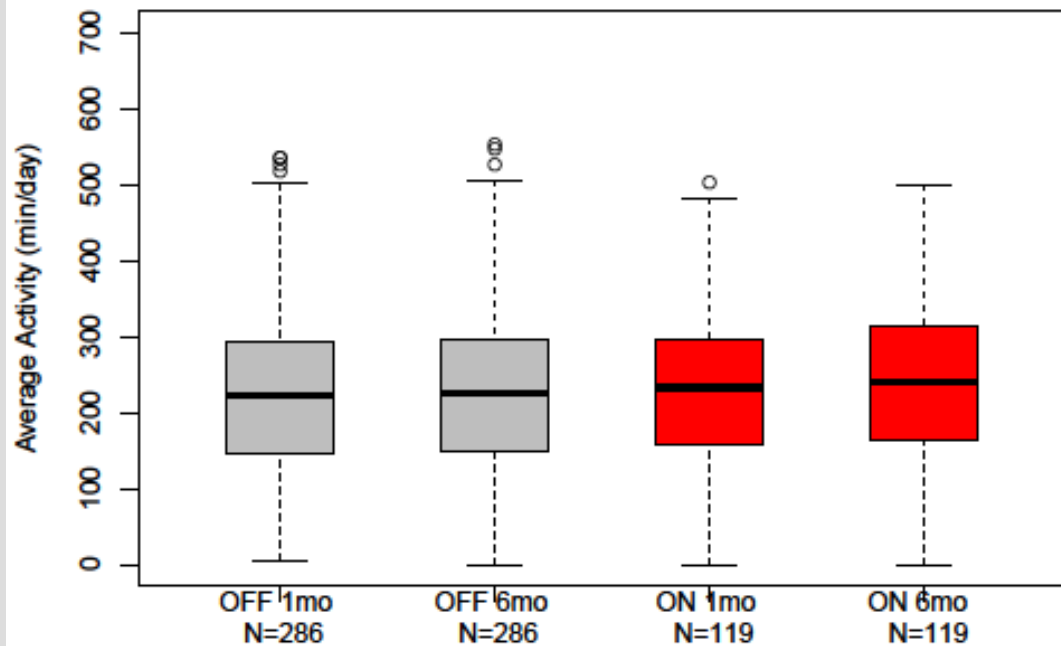
THANK YOU

- Any questions?

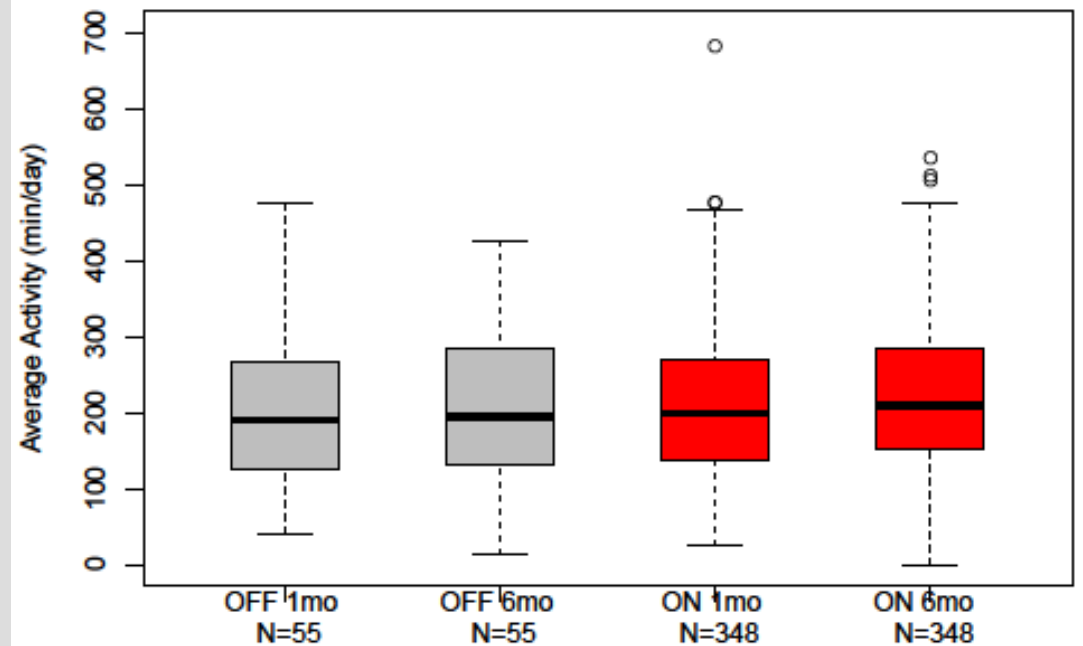
BACK UP SLIDES

SUBGROUP ANALYSIS: RATE RESPONSE PROGRAMMING

RAFT/REVERSE Without rate response programming throughout

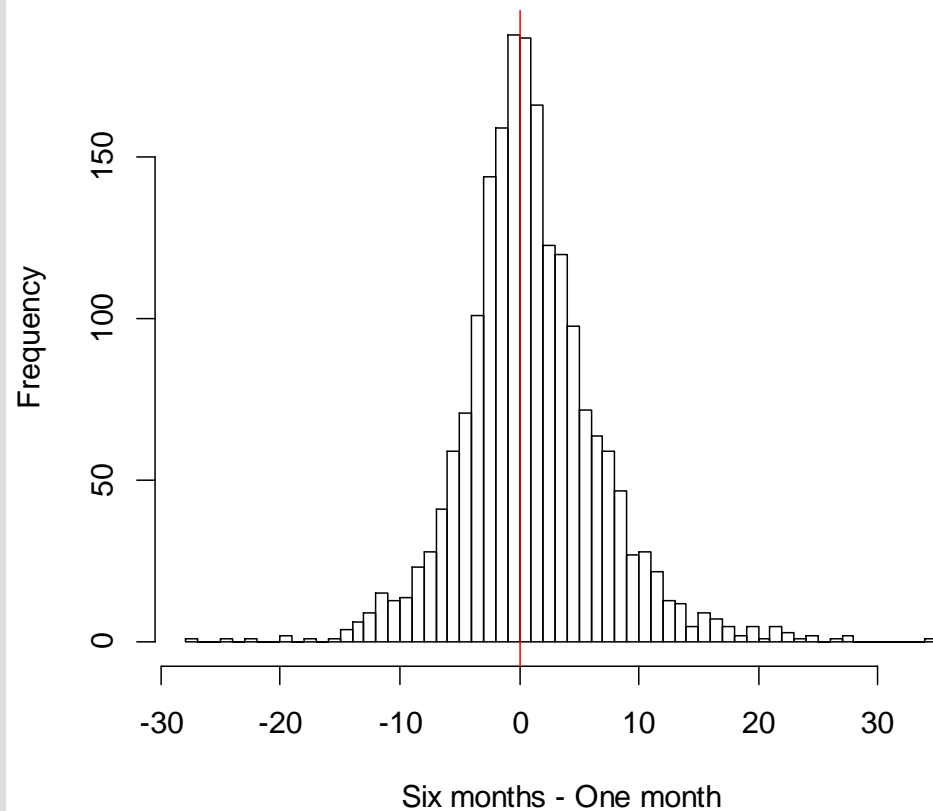


RAFT/REVERSE With rate response programming throughout



CHANGE IN PA FROM 1 MONTH TO 6 MONTHS

Distribution of the change in activity over time



	CRT OFF (N=1059)	CRT ON (N=1279)
1 month PA (Mean ± SD)	202 ± 107 min/day	207 ± 100 min/day
6 month PA (Mean ± SD)	213 ± 112 min/day	218 ± 105 min/day
Change from 1 to 6 months (Mean ± SD)	1.0 ± 5.9 min/day	1.1 ± 5.8 min/day
Percent with an increase in activity	55%	55%
Percent with a decrease in activity	45%	45%