The safety, feasibility and optimization of multiple prolonged breath-holds (> 5 minutes) in radiotherapy.

Dr Michael Parkes, respiratory physiologist, expertise on breath-holding

Member of a multidisciplinary radiotherapy team, national and international collaborations

Some of our work is supported by Accuray Inc, (California).

The problem- patients breathe during radiotherapy.

Thoracic and abdominal tumours can move by up to 3.5 cm per breath.
So some healthy tissue has to be irradiated to guarantee irradiation of all the tumour.

We are attempting to solve this problem using a mechanical ventilator to

- **impose a regularized breathing pattern**
- **enable single or multiple prolonged breath-holds (> 5 minutes)**

Mechanical ventilation of <u>conscious & unmedicated</u> patients is easy.

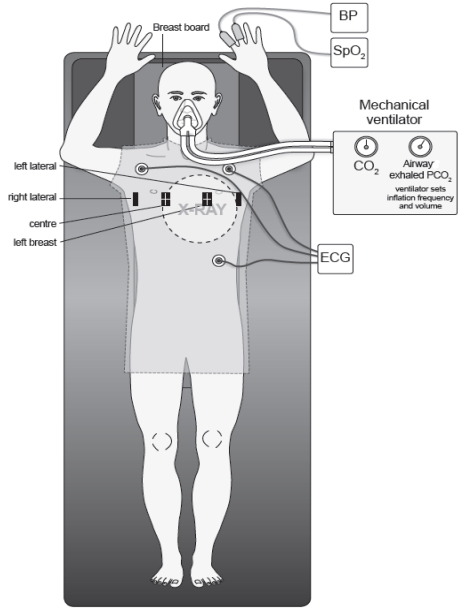
Connected to a ventilator via facemask, initially breathing spontaneously.

Switch ventilator to positive pressure ventilation.
Ventilator now completely takes over their breathing.
(Subjects don't use their diaphragm).

Takes about 1 minute to learn!
Others are now using it (Van Ootgehem [Louvain] 2019, Green Journal)

<u>Advantages of mechanical ventilation</u>
Ethics ✓<u>non-invasive</u>
Completely safe because patients can remove the mask at any time.
Patients <u>do nothing</u>…….. (they require no feedback)……
….music..... often fall asleep.....
Can ventilate them for up to 1 hour (then get bored and restless).

supine patient



Parkes et al, 2016a&b BJR
http://dx.doi.org/10.1259/bjr.20150741
http://dx.doi.org/10.1259/bjr.20160199

Personalized Radiotherapy Delivery

What mechanical ventilation pattern is most comfortable for the patient?
What target organ motion do treatment planners want?

Slow deep ventilation (*e.g.,* 3 breaths per min. @ 1.8L).
The target is predictably stationary between breaths,
(but when it moves, the movement is big).

Multiple short breath-holds will become obselete!
Instead just use the mechanical ventilator for 2½ minutes!

Rapid shallow ventilation (*e.g.,* 25 breaths per min. @0.2L)
The target is always moving predictably,
(but **small movements)**

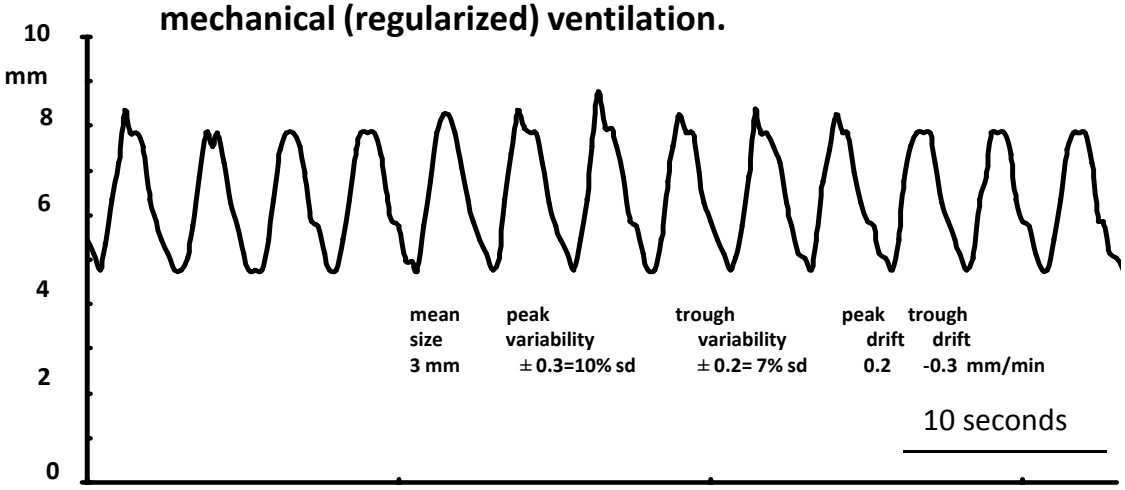
"realistic ambition" of
< ± 1 mm chest surface movement per breath
not cm!

Mechanical ventilation regularizes patient's breathing and minimizes its variability

Parkes *et al.,* (2016) BJR

http://dx.doi.org/10.1259/bjr.20150741

Left breast ant.-post. surface movement during 50s of mechanical (regularized) ventilation.



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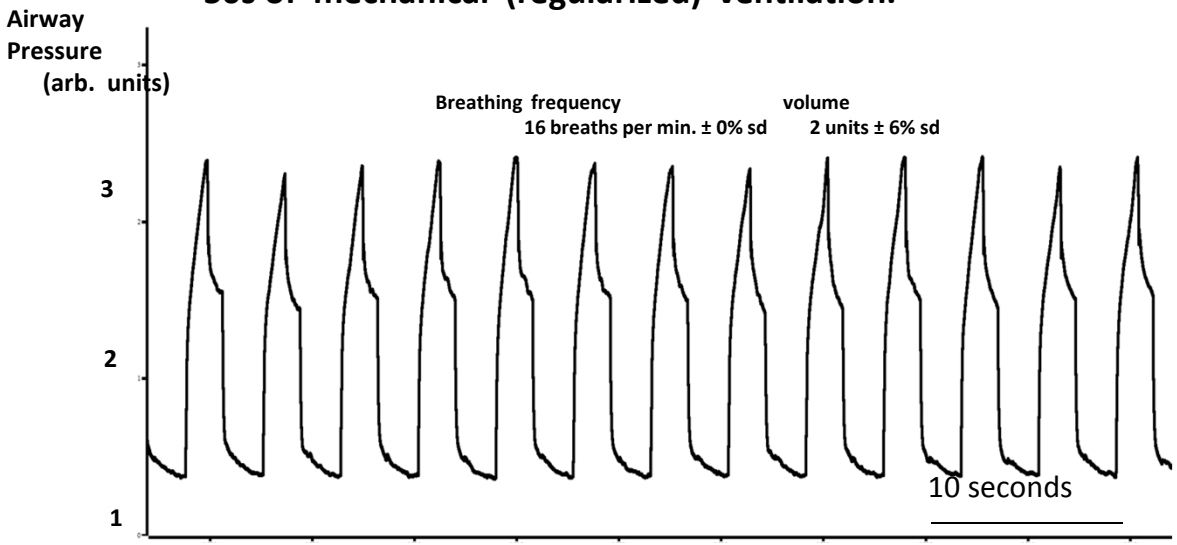
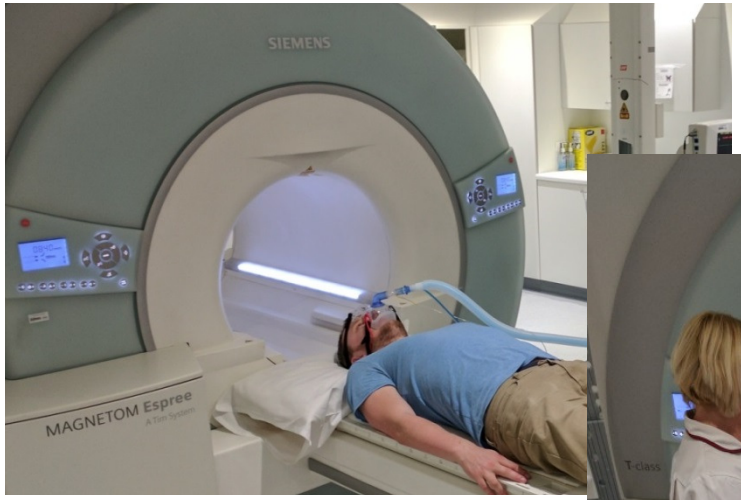


Mechanical ventilation to reduce internal respiratory movement and its variability.

West, Parkes *et al.*, 2018 Red Journal.
https://doi.org/10.1016/j.ijrobp.2018.11.040



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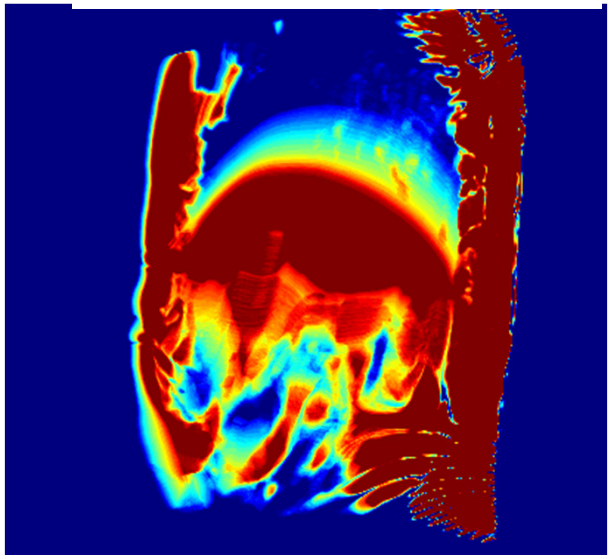
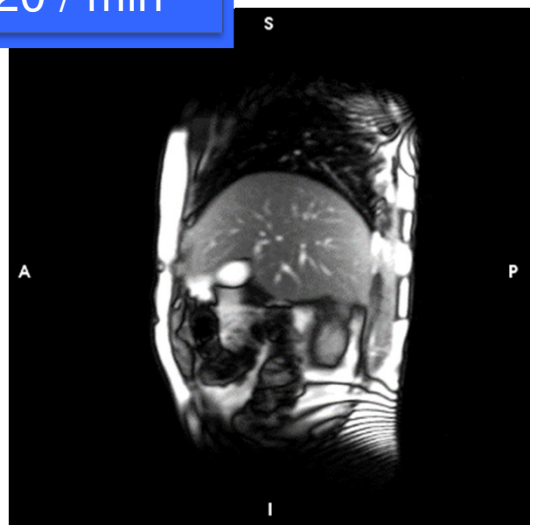
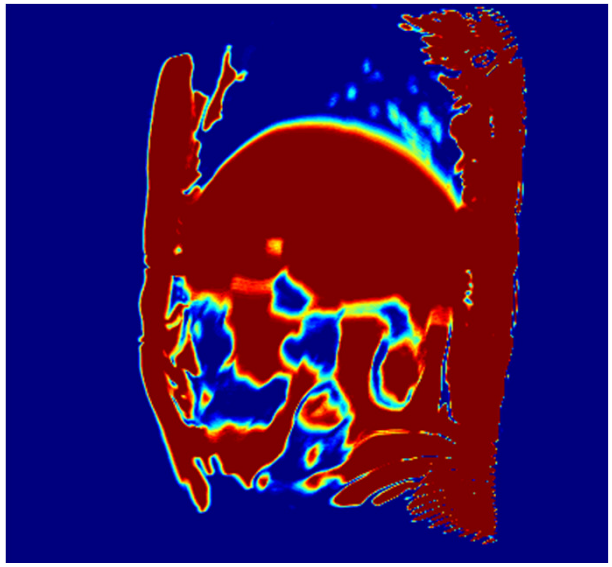
Eupnea



20 / min





Mechanical ventilation reduces internal respiratory movement amplitude and reduces its variability. **West, Parkes *et al.*, 2018 Red Journal.**

https://doi.org/10.1016/j.ijrobp.2018.11.040

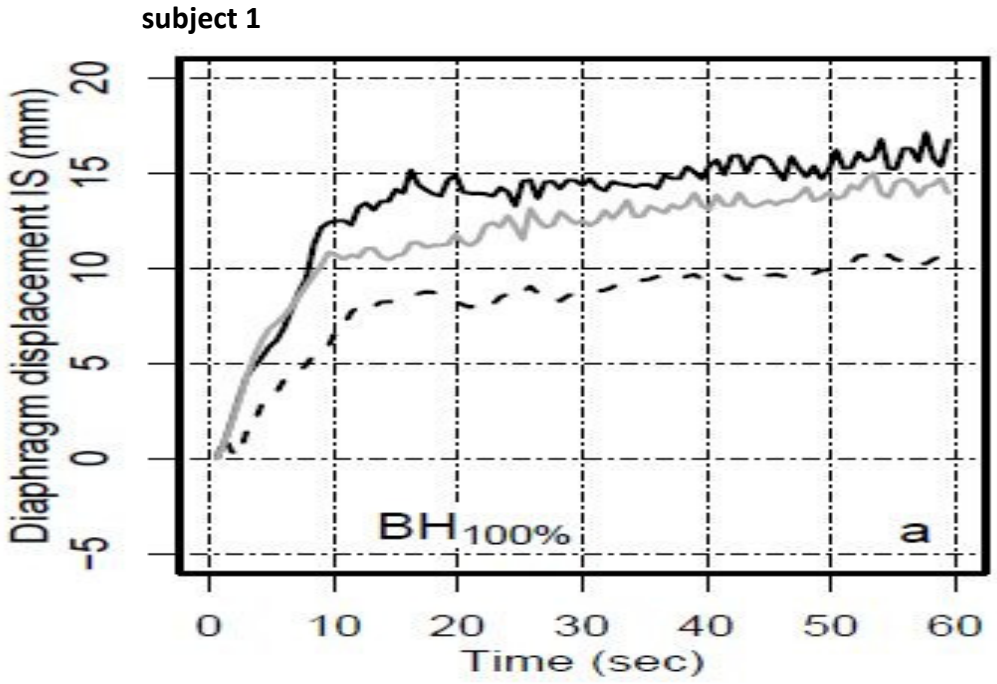
AMC Amsterdam

Multiple (10?), short (20 second?) breath-holds are now being introduced (Bartlett et al., 2015 Green Journal) .

They produce clear heart and lung dosimetric benefits for breast cancer
(Boda-Heggemann et al., 2016 Red Journal).

Naive to assume that breath-holding stops all internal organ movement because

a) diaphragm "settles" 10-15mm over the first ~15 sec of a short breath-hold



MRI of the diaphragm during 3 short breath-holds

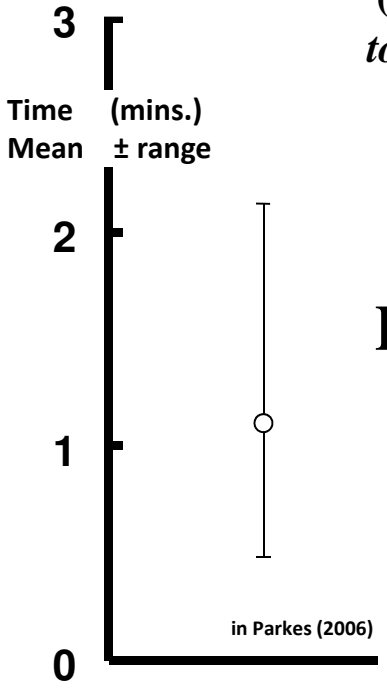
Lens, Parkes et al., (2016) Green Journal
http://dx.doi.org/10.1016/j.radonc.2016.09.012

b) chest must shrink linearly throughout all breath-holds
because not every gas molecule of O_2 absorbed can be replaced by gaseous CO_2
(breath-holding reduces the pressure gradients removing CO_2 from blood)

No problem because patients can safely breath-hold for much longer than 20 seconds!

What is normal breath-hold duration? Parkes 2006

http://onlinelibrary.wiley.com/doi/10.1113/expphysiol.2005.031625/abstract



318 subjects
Schneider (1930)
Breath-hold from air, max inflation

(Schneider, 1930) ***"it is practically impossible for a man at sea level to voluntarily hold his breath until he becomes unconscious."***

Simple safety precautions to ensure it will never happen.

Additionally, practice improves breath-hold duration by ~30%
distraction improves breath-hold duration by ~20%

Preoxygenation (60% O_2) doubles breath-hold duration.

(makes more O_2 available)

Why isn't everyone in radiotherapy already using this?! **(instead of air = 21% O_2)** **Historical!**

Hypocapnia doubles breath-hold duration.

(Halve the CO_2 content of blood so it can absorb more CO_2)

Hyperventilation → hypocapnia.

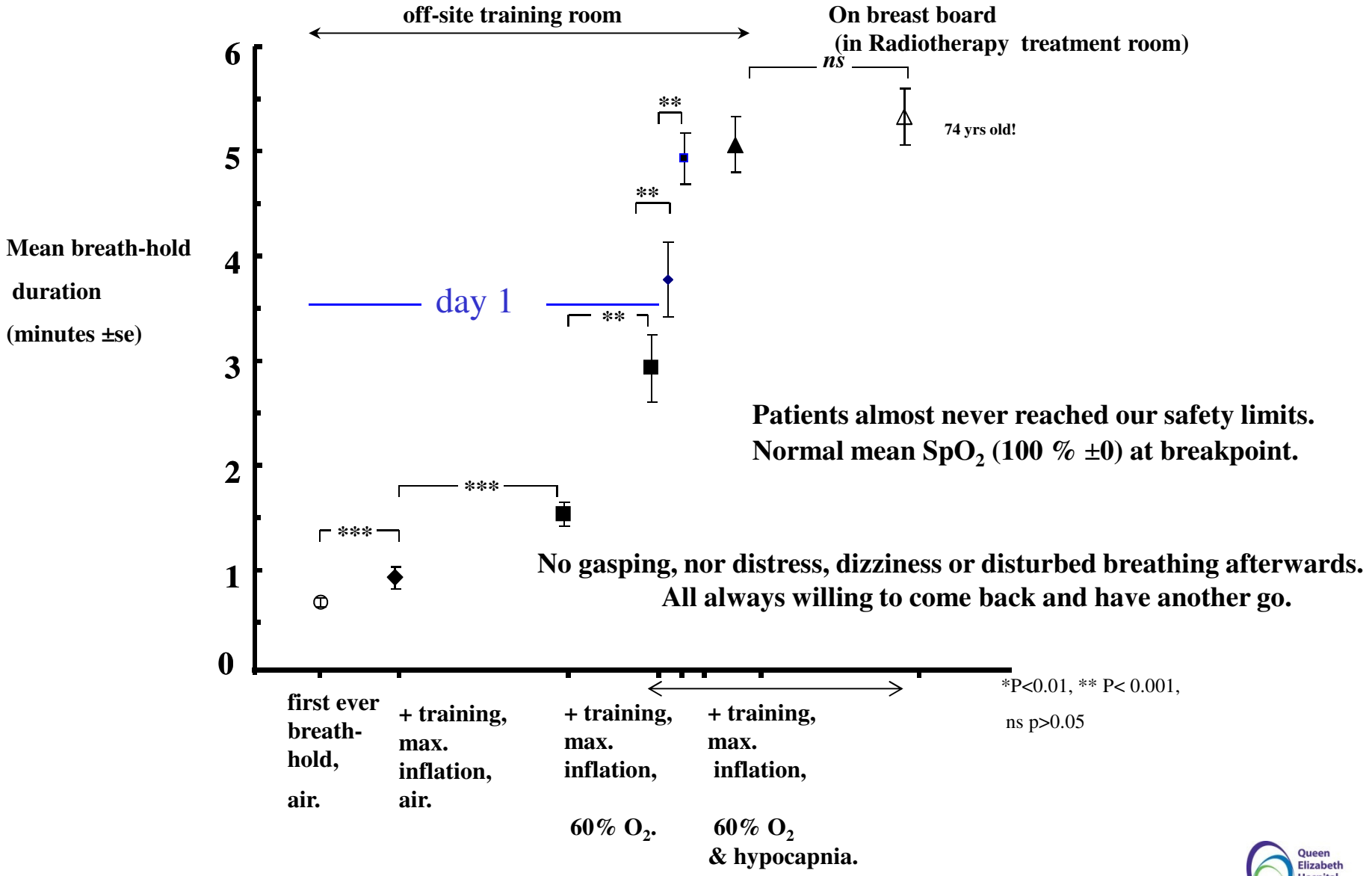
Voluntary hyperventilation is too difficult & unsafe for patients.

Mechanical hyperventilation is safe and easy for patients.

So combine mechanical hypocapnia and preoxygenation!

The single prolonged breath-hold in 15 breast cancer patients (Parkes 2016 BJR)

http://www.birpublications.org/doi/10.1259/bjr.20160194



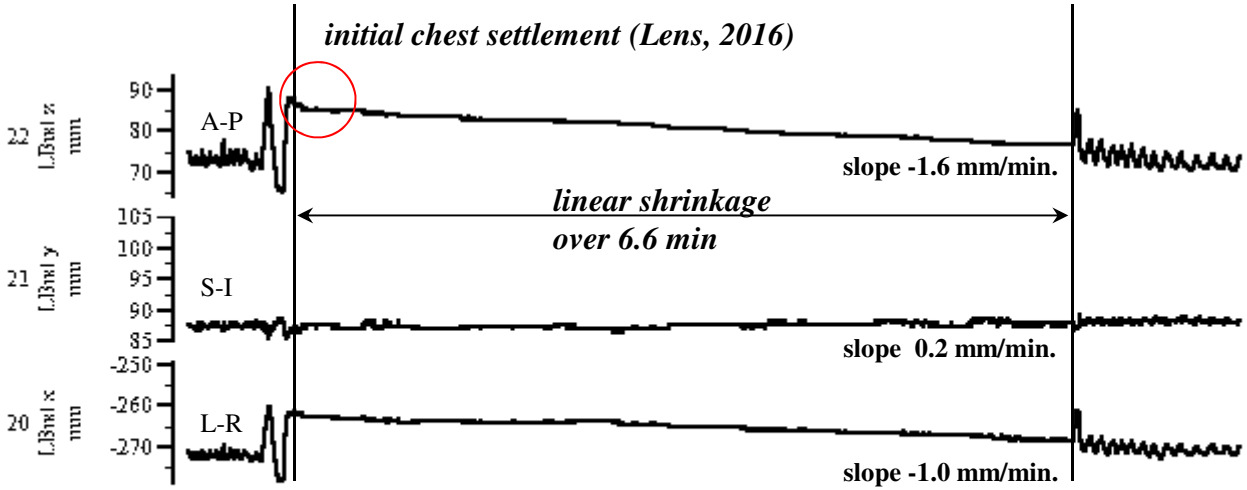
Queen Elizabeth Hospital Birmingham Charity
www.qehb.org

The expected small, linear chest shrinkage during single prolonged breath-holds

At present!

Parkes 2016a, BJR
http://dx.doi.org/10.1259/bjr.20150741

Surface marker movement measured during the longest breath-hold (6.6 minutes) on the breastboard.



We have patented a method using the ventilator to abolish this linear shrinkage.

Also no reason why children (aged ≥8 years) shouldn't be able to perform single prolonged breath-holds for >5 minutes.

Also can perform single prolonged breath-holds in the prone position (Parkes & De Neve [UZGent] 2019, manuscript in preparation).

Multiple short breath-holds, so why not <u>multiple</u> <u>prolonged</u> breath holds?

Parkes, et al., 2019, Green Journal submitted

Measure their single prolonged breath-hold duration.
Order them to break at an <u>arbitrary</u> 80% of this duration, take one breath of 60% O_2 & breath-hold again.
How long is the second breath-hold?

3 minute 2nd breath-hold after relieving the first with a single breath of 60% O_2.

How is this possible?

At the 1st (80%) breakpoint (= start of 2nd breath-hold),
sPO_2 still 99% ±0 & normocapnic $P_{et}CO_2$ = 45 ±1 mmHg.

Have also relaxed and so started re-reperfusion of the diaphragm.

Multiple short breath-holds, so why not <u>multiple</u> <u>prolonged</u> breath holds?

Parkes, et al., 2019, Green Journal submitted

Measure their single prolonged breath-hold duration.
Order them to break at an <u>arbitrary</u> 80% of this duration, re-hyperventilated in 60% O_2 for 3 minutes & breath-hold again.
How long is the second breath-hold?

6 minute 2nd breath-hold by re-introducing 60% O_2 and hypocapnia.

How is this possible?

At the start of 2nd breath-hold,
sPO_2 99% ±0, hypocapnic $P_{et}CO_2$ = 20 ±0 mmHg, diaphragm is completely reperfused.

Multiple short breath-holds, so why not multiple prolonged breath holds?

Measure their single prolonged breath-hold duration **Parkes, et al., 2019 Green journal, submitted**

Order them to break at an arbitrary 70% of this duration, re-hyperventilated in 60% O_2 for 3 minutes & breath-hold again.

Can subjects repeat this 9 times easily and safely? **YES!**

9 successive prolonged breath-holds totalling 41 minutes.

Breath-hold time = potential treatment time.

So we could deliver safely 41 minutes of radiotherapy treatment time in a single 66 minute session using multiple prolonged breath-holds.

Multiple short breath-holds will become obselete!

Conclusions

We can safely use a mechanical ventilator on breast cancer patients to regularize breathing and impose breathing patterns from slow deep to rapid shallow.

We can safely us a mechanical ventilator to achieve
single prolonged breath-holds of > 5 minutes in breast cancer patients.

We can now safely achieve multiple prolonged breath-holds
giving 41 minutes of radiotherapy treatment time in a 66 minute session.

We are happy to collaborate to develop and introduce these techniques
into photon and proton radiotherapy
throughout Europe.