Complete control of respiratory motion: mechanical ventilation is the way forward for Radiotherapy and Medical Imaging.
Multidisciplinary team

– Dr Michael Parkes, Physiologist,
– Prof Stuart Green, Dr Jason Cashmore, Medical Physics
– Dr Tom Clutton-Brock, Anaesthesia + Intensive Care Medicine
– Dr Qamar Ghafoor Oncology (lung cancer)
– Dr Andrea Stevens Oncology (breast cancer)
– Dr Arjan Bel- Academic Medisch Centrum, Amsterdam

Key points

• A mechanical ventilator can now take complete control of a conscious/unmedicated patient’s breathing & regularize it for ~ 1 hour
  Parkes (2016).
  Reducing the within-patient variability of breathing for radiotherapy delivery in conscious, unseparated cancer patients using a mechanical ventilator.
  Br J Radiol 89, 20150741.

• Patients can breath-hold safely for ten times longer (>5 minutes) than currently asked to do (~ 20 secs)
  (with help from a mechanical ventilator)
  Parkes (2016a&b).
  Safely achieving single breath-holds of >5 minutes in cancer patients: feasibility and applications for radiotherapy.
  Br J Radiol 89, 20160194

• Consider how we might best apply mechanical ventilation to photon & proton beam delivery.
Clinical justification for our research

The major problem in radiotherapy and diagnostic imaging :-

• Patients breathe during radiotherapy, thoracic and abdominal tumours move by up to 3.5cm
  → so healthy tissue has to be irradiated to guarantee irradiation of all tumour,
  → healthy tissue damage - L breast cancer (heart) and other vital tissues.

Examples of movement:-
Current attempts to solve the respiratory motion problem

1. Ignore the breathing and irradiate the entire movement path beyond the tumour to guarantee treating the tumour.

2. Abdominal compression to restrict the range of motion during breathing.

3. Gate treatment within the breathing cycle

4. Tumour tracking strategies

5. Repeated treatments during multiple short (~20 secs) breath-holds (DIBH).

- Current Radiotherapy concept of a breath-hold does not correspond with basic physiology.

- ~22 s breath-hold (Roth, 2011) = regular breathing at ~3 times a minute!

- We physiologists measure breath-holds in minutes.
We use a mechanical ventilator to offer two novel & “revolutionary” solutions

1. Train the patient to let a mechanical ventilator take complete control of their breathing, Parkes (2016).

The ventilator then delivers regularized breaths of constant frequency & volume.

The ventilator makes tumour movement predictable & improves tracking prediction of tumour position (and hence dealing with any lag issues).

The ventilator could even feed forward to an accelerator, “telling” the accelerator where the tumour will be to treat predetermined tissue volumes.

2. Could give each entire radiotherapy treatment session in a single prolonged breath-hold (>5 minutes), Parkes (2016a&b).

Use a ventilator to hyperventilate to cause hypocapnia (and add 60% oxygen to inspired gas) to perform one single >5 minute breath-hold-

Abolishes all rhythmic breathing movements in the treatment session.

Why haven’t single prolonged breath-holds been considered before?

Breath-hold physiology not taught at medical school.

...............because prolonged breath-holds had no clinical application....

Physiologist...........

...for the first time, single prolonged breath-holds could have a major clinical application in radiotherapy and imaging.
**Part 1. What is normal breath-hold duration?**

*Can you breath-hold until you pass out? No!*  
(Schneider, 1930) “it is practically impossible for a man at sea level to voluntarily hold his breath until he becomes unconscious”

No! Never seen it. Nor reported. **Competitive breath-hold divers.**

Simple safety precautions to ensure it will never happen.

Useful knowledge to reassure patients.

---

A.  
318 USAF pilots  
Schneider (1930)  
*Breath-hold from air, max inflation*

1 minute breath-hold is just a starting point ............
Single prolonged breath-holds (with preoxygenation and hypocapnia) are safe.

During a single ~9 minute breath-hold— not much happens! (Parkes 2014)

12 inexperienced healthy subjects, mean breath-hold duration 5.5 ±0.5se min.
Normal mean blood gases at breakpoint (still 98% $O_2$ saturated, normal PetCO$_2$ levels (43 ± 2 se mmHg) mean sBP 166±4 mmHg).
No gasping, no distress, no dizziness nor disturbed breathing in the post breath-hold period.

We defined safety limits for patients for single prolonged breath-holds.
Safety equipment- monitor SpO$_2$ and blood pressure non-invasively.
Stop if SpO$_2$ < 94% or sBP > 180 mmHg.

Parkes (2014) BJR
http://dx.doi.org/10.1259/bjr.20140454
The key to breath-holding appears to lie in the diaphragm muscle.

But almost nothing is known about the physiology of the diaphragm muscle, because it is so inaccessible.

Why is the diaphragm important for breath-holding in Radiotherapy?

Because patients feel safe learning to fight a sensation from a muscle!

(They would be much more cautious if they were fighting the sensation of asphyxia!)
How long can cancer patients perform a single breath-hold? (Parkes, 2016a)

N=15 female patients with breast cancer (.... available).

Volunteer patients. Aged 37-75 (average 54, 4 were 60+).

Exclusion criteria
no hypertension, no coronary artery disease,
non-smokers, no asthma
no obesity, no epilepsy
no diabetes. very cautious! …

All undergoing radiotherapy
(each experiment preceded by a treatment session),

12 had undergone chemotherapy (2 with Herceptin).

Conscious, unmedicated, lying listening to music

Deliberately mechanically hyperventilate (over-ventilate)
to induce safe hypocapnia, (drop PCO₂ from ~40 to 20 mmHg) and preoxygenate (inhale 60% O₂).

Then switch off the ventilator and tell the patient to inhale and breath-hold (with mask still on).
Mean duration of single breath-holds in 15 cancer patients (Parkes 2016a)

Patients almost never reached our safety limits.

Normal mean blood gases at breakpoint
\(\text{SpO}_2 = 100 \pm 0 \text{ se } \%\), \(\text{PetCO}_2 = 35 \pm 2 \text{ se mmHg}\)

sBP at breakpoint 168 ± 4 mmHg

So no gasping, no distress, dizziness nor disturbed breathing afterwards.
Always willing to come back each time and have another go.

Parkes et al, 2016b
No rhythmic chest movement during breath-holding, but all thoracic and abdominal organs will move slightly!

• Some non-rhythmic movement continues during breath-holding because
  • 1). Initial settlement of the diaphragm and organs at the start of breath-holding
  • 2). Lungs deflate slowly by ~ 250 ml/min.
  • why?
  • (gaseous O₂ is extracted from alveolar air, but cannot be replaced by equal amounts of gaseous CO₂ returning from venous blood, because alveoli are no longer refreshed, so there is no partial pressure gradient)

• Importance in Radiotherapy for all breath-holds.
• Presumption that tumours make no movement during breath-holding- incorrect.
• But much less movement than during free breathing.

• Emerging data showing clear heart and lung dosimetric benefits for breast cancer of multiple short breath-holds (DIBH)

• We think the single prolonged breath-hold of >5 minutes has much more to offer.


Small linear chest shrinkage during single prolonged breath-holds (Parkes 2016a)

Polygraph record of the longest breath-hold (6.6 minutes) under simulated treatment conditions. (markers on shirt)

<table>
<thead>
<tr>
<th></th>
<th>mean mm/min</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean anterior-posterior (z)</strong> movement of L breast marker</td>
<td>-1.9 ± 0.3 mm/min, n=15</td>
</tr>
<tr>
<td><strong>Mean superior-inferior (y)</strong> movement of all markers</td>
<td>0.1 ± 0.1 mm/min, n=11</td>
</tr>
<tr>
<td><strong>Mean left-right (x) movement of all markers</strong></td>
<td>-0.6 ± 0.2 mm/min, n=11</td>
</tr>
</tbody>
</table>
Initial organ settlement during multiple short breath-holds (Lens et al., 2016)

MRI of the diaphragm and pancreatic head during multiple short breath-holds from air (DIBH) with different inflation volumes (0-100% inspiratory capacity) in 16 healthy volunteers.

Train .... even simpler just to mechanical ventilation during radiotherapy
we already have the data ............

Mechanical ventilation regularizes breathing and breast movement in patient 1.

For n=15 patients, during mechanical ventilation at 16 breaths per minute
with the increased inflation volume necessary to cause hypocapnia,
mean rhythmic A-P marker movement
is ±2.5 ± 1mm.

Mean variability in
peak position marker is 0.5 ±0.1 mm,
trough position marker is 0.4 ±0.0 mm,
marker position drift is n.s. from zero.

Mechanical ventilation achieved an
85% reduction in mean within-breath variability (sd) of breathing frequency (P<0.05)
29% reduction in mean within-breath variability (sd) of breath “volume” (P<0.05)

But we allowed patients to override the ventilator
(they like the freedom to cough or sigh or talk or laugh)
If we instruct the patients never to override the ventilator,
the reduction in variability will be even greater.
Possibility of Synchronizing the ventilator with Accelerator or imaging equipment.

Breathing pattern feeding forward to accelerator

Ventilator sets breathing pattern

Feedback

accelerator

ventilators over-engineered

We are currently raising funds to develop a customised “radiotherapy ventilator”.

Target cost £5000 per ventilator

Dual usage- regularized ventilation

single prolonged breath-hold

A number of companies are interested

Patient

Patient breathing pattern monitor

Treatment
Conclusions-

Complete control of respiratory motion: mechanical ventilation is the way forward for Radiotherapy and Medical Imaging.

Shown how a mechanical ventilator can now
1) take complete control of patient’s breathing for ~1 hour Parkes (2016).

2) have patients performing a single prolonged breath-hold for > 5 minutes Parkes (2016a&b).

Educate ……………… resistance ……..

How best we might apply mechanical ventilation to photon and proton beam delivery?
Recent breath-holding publications


Complete control of respiratory motion: mechanical ventilation is the way forward for Radiotherapy and Medical Imaging.