A Randomised Phase II Trial of Standard -vs- Dose Escalated Radiotherapy for the Treatment of Malignant Pleural Mesothelioma

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Malignant Pleural Mesothelioma (MPM)
A cancer originating in mesothelial cells (lining) of the lung and typically caused by exposure to asbestos.

SYSTEMS-2 Randomised Clinical Trial
Phase II study comparing two schedules of hypofractionated radiotherapy. 6 Gy/# used in palliative treatment of locally advanced breast cancer. **Trial Hypothesis:** Increasing total radiotherapy dose and dose per fraction will increase the proportion of patients with MPM that experience a clinically significant improvement in pain 5 weeks after treatment.

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<th>SYSTEMS-2 (Study Design)</th>
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<tr>
<td>Control Arm (n = 56)</td>
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<td>20 Gy in 5+ (One Week)</td>
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<td>Treatment Arm (n = 56)</td>
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<td>36 Gy in 6+ (Two Weeks)</td>
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Why SYSTEMS-2 in Glasgow?
Glasgow, which is famous for shipbuilding, is a hotspot for MPM. Picture below of iconic Titan, which played a leading role in the shipbuilding industry at Clydebank in Glasgow.

Management of MPM
Poor prognosis with a median survival time of approximately nine months. Surgery involves removal of some or all of the pleura and perhaps part of the lung.

Palliative radiotherapy regarded as the standard treatment option for pain control. Difficult to target PTV in conjunction with sparing OARs through AP/PA technique.

VMAT treatment planning postulated to be a positive step forward whereby higher conformal doses may be delivered to the PTV while minimising unwanted dose to OARs and reducing the risk of significant acute toxicity.

SYSTEMS-2 initiated as there is a clinical unmet need to improve the quality of life of patients presenting with MPM.

Results
Currently, eight patients have been recruited to SYSTEMS-2. Figure below illustrates % Dose to PTV for each individual patient for 36 Gy in 6# plans.

PTV and OAR volumes were recorded and shown below. Mean PTV volume = 1109 cc.

Why is Asbestos so devastating?
Asbestos is a naturally occurring mineral in the form of spindly fibres. Flexible, strong and fire retardant. Shape and size affords easy admission into the lungs. Fibres accumulate, cause scarring, inflammation and symptomatic diseases with latency periods of 30-40 years.

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Incidence of MPM
Higher in UK compared to anywhere in the world. UK asbestos deaths approximately 2,500 per year. Incidence predicted to increase over next five years.

Conclusion
The palliative care of patients presenting with MPM is required now more than ever due to increasing incidences. Treatment planning employing the RapidArc® technique offers precise targeting of the PTV while minimising OAR dose and consequently reducing the risk of significant acute toxicities often seen with conventional techniques. Palliative hypo-fractionated radiotherapy serves as an invaluable treatment for patient’s presenting with MPM as it offers an augmented quality of life unrivaled by any other treatment modality.

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Dose Constraints using the UK SABR consortium guidelines

For example, the Queen Elizabeth II was built here between 1965-67. Shipyards were a main exposure point of asbestos, which was used for insulation on ships.

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**PARTICLEs that are respirable to deep parts of the lung < 10 µm**

- Asbestos
- Hair
- Bacteria
- Smog
- Tobacco Smoke

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