Appendix 1 Searching

## Databases searched for studies of FI for RMS

<table>
<thead>
<tr>
<th>Databases searched for studies of FI for RMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MEDLINE and MEDLINE In-Process (via Ovid, 1946 to present, searched 30/October/2013);</td>
</tr>
<tr>
<td>• CENTRAL (Cochrane Central) Register of Controlled Trials (via Cochrane Library. CENTRAL issue 9 of 12 September 2013. Searched 30/October/2013);</td>
</tr>
<tr>
<td>• Clinical Trials.gov (via <a href="http://clinicaltrials.gov/">http://clinicaltrials.gov/</a>, Searched 30/October/2013);</td>
</tr>
<tr>
<td>• EMBASE (Excerpta Medical Database) (via OVID SP 1974 to 2013 October 29&gt;, searched 30/October/2013);</td>
</tr>
<tr>
<td>• HTA database (via CRD website: <a href="http://www.crd.york.ac.uk/crdweb/HomePage.asp">http://www.crd.york.ac.uk/crdweb/HomePage.asp</a>, searched 30/October/2013);</td>
</tr>
<tr>
<td>• International Cancer Research Partnership (ICRP) (via <a href="https://www.icrpartnership.org/database.cfm">https://www.icrpartnership.org/database.cfm</a>, searched 05/November/2013);</td>
</tr>
<tr>
<td>• metaRegister of Controlled Trials (mRCT) active registers (via <a href="http://www.controlled-trials.com/mrct/search.html">http://www.controlled-trials.com/mrct/search.html</a>, searched 14/November/2013);</td>
</tr>
<tr>
<td>• PubMed (via <a href="http://www.ncbi.nlm.nih.gov/pubmed/advanced">http://www.ncbi.nlm.nih.gov/pubmed/advanced</a>, searched 08/November/2013);</td>
</tr>
</tbody>
</table>

## Databases searched for systematic reviews of FI for cancer

<table>
<thead>
<tr>
<th>Databases searched for systematic reviews of FI for cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CDSR (Cochrane Database of Systematic Reviews) (via Cochrane Library. CDSR issue 11 of 12 November 2013. Searched 05/November/2013);</td>
</tr>
<tr>
<td>• DARE—Database of Abstracts of Reviews of Effects (via CRD website, <a href="http://www.crd.york.ac.uk/CRDWeb/">http://www.crd.york.ac.uk/CRDWeb/</a>, Searched 05/November/2013);</td>
</tr>
</tbody>
</table>

## Searches for studies of functional imaging for RMS:

**Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>**

Searched 30-10-2013

Annotated search strategy:

-------------------------------------------------------------------------------

1 Rhabdomyosarcoma, Alveolar/ or Rhabdomyosarcoma/ or Rhabdomyosarcoma, Embryonal/ (9170)

2 Rhabdomyosarcoma*.ti,ab. (9377)

3 1 or 2 (12196)

**Line 3 captures terms for rhabdomyosarcoma (RMS)**

4 positron-emission tomography/ or "positron-emission tomography and computed tomography"/ (31876)

5 (photon emission adj3 tomograph*).ti,ab. (14192)

6 (positron emission adj3 tomograph*).ti,ab. (36244)
Line 13 captures terms for Positron Emission Tomography (PET)

Line 14 combines terms for PET and RMS

Line 15 captures terms for Magnetic Resonance Imaging (MRI)

Line 22 combines terms for MRI and RMS

Line 27 captures terms for spectroscopy
Line 28 combines terms for spectroscopy and RMS

29  dcemri*.ti,ab. (30)

30  functional imag*.ti,ab. (7644)

31  or/29-30 (7672)

Line 31 captures terms for functional imaging

32  31 and 3 (3)

Line 32 combines terms for functional imaging and RMS

33  14 or 22 or 28 or 32 (666)

Line 33 brings together all the records identified for the various different types of functional imaging

CENTRAL (Cochrane Central Register of Controlled Trials) (via Cochrane Library. CENTRAL issue 9 of 12 September 2013. Searched 30/October/2013);

Search strategy:

#1  [mh ^"Rhabdomyosarcoma, Alveolar"] or [mh ^"Rhabdomyosarcoma, Embryonal"] or [mh ^Rhabdomyosarcoma] in Trials 51

#2  Rhabdomyosarcoma* in Trials 90

#3  {or #1-#2} 90

Clinical Trials.gov (via http://clinicaltrials.gov/, Searched 14/November/13)

Search strategy:

rhabdomyosarcoma* and (tomograph* OR PET* OR SPECT* OR “magnetic resonance*” OR MRI OR MRIs OR spectroscop* or “functional imag* or Fluorodeoxyglucose” OR dcemri*) – 10 records

EMBASE (Excerpta Medical Database) (via OVID SP 1974 to 2013 October 29>, searched 30/October/13)
Search Strategy:

1. rhabdomyosarcoma/ or embryonal rhabdomyosarcoma/ (13925)
2. Rhabdomyosarcoma*.ti,ab. (11270)
3. or/1-2 (16101)
4. positron emission tomography/ (80086)
5. computer assisted emission tomography/ (16482)
6. (photon emission adj3 tomograph*).ti,ab. (16812)
7. (positron emission adj3 tomograph*).ti,ab. (44186)
8. pet.ti,ab. (80248)
9. spect.ti,ab. (29923)
10. Fluorodeoxyglucose F18/ (33010)
11. Fluorodeoxyglucose.ti,ab. (11286)
12. (18-fdg or fdg-18 or 18f-fdg or fdg-18f).ti,ab. (11612)
13. (18fdg or fdg18 or 18ffdg or fdg18f).ti,ab. (1984)
14. or/4-13 (156421)
15. 14 and 3 (309)
16. nuclear magnetic resonance imaging/ or diffusion tensor imaging/ or diffusion weighted imaging/ (459617)
17. magnetic resonance imag*.ti,ab. (161366)
18. (MRI or MRIs).ti,ab. (199744)
19. (MR or MRs).ti,ab. (131475)
20. (diffusion adj4 (imag* or tractograph*)).ti,ab. (20139)
21. magnetic resonance tractograph*.ti,ab. (36)
22. or/16-21 (571190)
23. 22 and 3 (1229)
24. nuclear magnetic resonance spectroscopy/ (98107)
25. electron spin resonance/ (32873)
26  spectroscop*.ti,ab. (232789)
27  nuclear magnetic resonance.ti,ab. (32396)
28  nmr*.ti,ab. (141440)
29  or/24-28 (386947)
30  3 and 29 (71)
31  dcmri*.ti,ab. (80)
32  functional imag*.ti,ab. (9444)
33  or/31-32 (9518)
34  33 and 3 (8)
35  15 or 23 or 30 or 34 (1432)

**HTA database (via CRD website: [http://www.crd.york.ac.uk/crdweb/HomePage.asp](http://www.crd.york.ac.uk/crdweb/HomePage.asp), searched 31/October/13)**

Search strategy:
1) MeSH DESCRIPTOR Rhabdomyosarcoma EXPLODE ALL TREES IN HTA 0 hits
2) ((rhabdomyosarcoma*)) and (Project record:ZDT OR Full publication record:ZDT) 1 hit
3) #1 OR #2 1 HIT

**International Cancer Research Partnership (ICRP) (via [https://www.icrpartnership.org/database.cfm](https://www.icrpartnership.org/database.cfm), searched 14/November/13)**

Search strategy:

**Containing All of These Words:** Rhabdomyosarcoma*


**CSO Codes:**
- 4.1 - Technology Development and/or Marker Discovery
- 4.2 - Technology and/or Marker Evaluation with Respect to Fundamental Parameters of Method
- 4.3 - Technology and/or Marker Testing in a Clinical Setting
- 4.4 - Resources and Infrastructure Related to Early Detection, Diagnosis or Prognosis
17 hits

**metaRegister of Controlled Trials (mRCT) active registers (via** [http://www.controlled-trials.com/mrct/search.html](http://www.controlled-trials.com/mrct/search.html), **searched 11/November/13)**

Search strategy:

Rhabdomyosarcoma* in all databases 46 hits


Search strategy:

#1   Search rhabdomyosarcoma[MeSH Terms]   8930
#2   Search Rhabdomyosarcoma, Alveolar[MeSH Terms]  558
#3   Search Rhabdomyosarcoma, Embryonal[MeSH Terms]  702
#4   Search Rhabdomyosarcoma*[Title/Abstract]  9174
#5   Search (#1 or #2 or #3 or #4)  11962
#10  Search ("photon emission" AND tomograph*[Title/Abstract])  14403
#11  Search (positron emission AND tomograph*[Title/Abstract])  36210
#12  Search pet[Title/Abstract]  53207
#13  Search spect[Title/Abstract]  20474
#15  Search "Fluorodeoxyglucose F18"[Mesh]  17448
#16  Search Fluorodeoxyglucose[Title/Abstract]  8566
#20  Search ("18-fdg" or "fdg-18" or "18f-fdg" or "fdg-18f"[Title/Abstract])  5387
#22  Search ("18fdg" or "f18g18" or "18gg18" or "fdg18f")[Title/Abstract])  702
#30  Search magnetic resonance imag*[Title/Abstract]  134446
#31  Search (MRI or MRIs[Title/Abstract])  371243
#32  Search (MR or MRs[Title/Abstract])  120807
#35  Search ((diffusion AND imag*) or (diffusion AND tractograph*)[Title/Abstract])  0
#36  Search magnetic resonance tractograph*[Title/Abstract]  28
    Search ("magnetic resonance spectroscopy"[Mesh] OR "nuclear magnetic resonance, biomolecular"[Mesh] OR "electron spin resonance spectroscopy"[Mesh] OR "nuclear magnetic resonance, biomolecular"[Mesh])  172389
#38  Search spectr*op*[Title/Abstract]  225674
#39  Search nuclear magnetic resonance[Title/Abstract]  29424
#40  Search nmr*[Title/Abstract]  118295
#41  Search dcemri*[Title/Abstract]  26
#42  Search functional imag*[Title/Abstract]  6839
    Search ((#9 or #10 or #11 or #12 or #13 or #15 or #16 or #20 or #22 or #30 or #31 or #32 or #35 or #38 or #39 or #40 or #41 or #42))  848762
#44  Search (#5 and #43)  663
Figure 1 Flow of studies through the review

Records identified through database and trial registers searching
n = 2313

Records after duplicates removed n = 1641

Records screened n = 1725

Records excluded n = 1418

Records unobtainable in full text n = 7

Full-text articles assessed for eligibility n = 300

Full-text excluded n = 285

Studies included in the review n = 8 (15 records)
Appendix 2: Quality assessment

Study Assessment tool

Possible answers for each criterion were “yes”, “no”, and where relevant, “unclear”, or “not applicable”.

- Were the selection/eligibility criteria adequately reported?
- Is the sample likely to be representative?
- Were patients recruited prospectively?
- Were patients recruited consecutively?
- Was the participation rate adequate (>80% of those eligible)
- Was there at least 80% follow-up from baseline?
- Was loss to follow-up reported?
- Were relevant prognostic factors reported? (e.g. histology, location of primary tumour)
- Were other relevant confounding factors reported? (e.g. excisional biopsy, variations in timing of imaging including variations in treatment point when imaging took place)
- Was an appropriate measure of variability reported?
- Was there an appropriate statistical analysis?
- Were there any other important limitations?
- Were the FI results assessed blind to the reference standard?
- Were the FI results assessed blind to the results of CI?
- Were there two independent assessors?
Intervention assessment criteria

Possible answers for each criterion were “yes”, “no”, and where relevant, “unclear”, or “not applicable”.

- Was the same scanner used for baseline and follow-up?
- Was residual activity in the syringe and injection tubing measured to accurately determine administered dose?
- Was an appropriate uptake time used (baseline minimum 60 minutes; baseline ± 10 minutes at follow-up)?
- Were acquisition technique and reconstruction parameters maintained for baseline and follow up; was the same CT protocol used?
- Were serum glucose and average liver SUV recorded before each PET?
- Were all patients weighed before imaging, at facility, using calibrated scale?
- Were dose calibrators calibration maintained and dose calibrator clocks synchronised with scanner clocks?
- Were screensaves or other documentation used to improve reproducibility in defining regions of interest between baseline and follow-up?
## Results of study quality assessment

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Baum (2011)</td>
<td>yes</td>
<td>unclear</td>
<td>no</td>
<td>unclear</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>unclear</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Dharmaramanjan (2012)</td>
<td>yes</td>
<td>unclear</td>
<td>no</td>
<td>unclear</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>unclear</td>
<td>unclear</td>
<td></td>
</tr>
<tr>
<td>Eugene (2012)</td>
<td>yes</td>
<td>yes</td>
<td>unclear</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Federico (2012)</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>unclear</td>
<td>NA</td>
<td>NA</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Klem (2007)</td>
<td>yes</td>
<td>unclear</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>unclear</td>
<td>yes</td>
<td>no</td>
<td>no*</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td></td>
</tr>
<tr>
<td>Ricard (2011)</td>
<td>yes</td>
<td>Yes ^</td>
<td>no</td>
<td>unclear</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Tateishi (2009)</td>
<td>yes</td>
<td>unclear</td>
<td>no</td>
<td>unclear</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Volker (2007)</td>
<td>yes</td>
<td>unclear</td>
<td>yes</td>
<td>unclear</td>
<td>NA</td>
<td>NA</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

*Those who had had chemotherapy and those who had not were analysed together. ^ but note atypical histology/gender balance
<table>
<thead>
<tr>
<th>Study</th>
<th>Same scanner used?</th>
<th>Administered dose accuracy?</th>
<th>Uptake time appropriate?</th>
<th>Acquisition technique/reconstruction parameters maintained?</th>
<th>Serum glucose and average liver SUV</th>
<th>Patient weighed adequately</th>
<th>Adequate calibration</th>
<th>Reproducibility of ROI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baum (2011)</td>
<td>NA</td>
<td>unclear</td>
<td>yes</td>
<td>NA</td>
<td>yes</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Dharmarajan (2012)</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Eugene (2012)</td>
<td>unclear</td>
<td>unclear</td>
<td>yes</td>
<td>yes</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>Unclear*</td>
</tr>
<tr>
<td>Federico (2012)</td>
<td>NA</td>
<td>unclear</td>
<td>Yes</td>
<td>NA</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Klem (2007)</td>
<td>NA</td>
<td>unclear</td>
<td>No†</td>
<td>NA</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Ricard (2011)</td>
<td>unclear</td>
<td>unclear</td>
<td>yes</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Tateishi (2009)</td>
<td>NA</td>
<td>unclear</td>
<td>yes</td>
<td>NA</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
<tr>
<td>Volker (2007)</td>
<td>NA</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
<td>unclear</td>
</tr>
</tbody>
</table>

*Blood glucose level was controlled but it is unclear if average liver SUV was recorded before each PET.45 to 60 minutes
### Appendix 3: Results of imaging of primary tumours

<table>
<thead>
<tr>
<th>Study</th>
<th>Image</th>
<th>N</th>
<th>Primary tumour imaging details</th>
<th>SUV(_{\text{max}}): mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baum (2011)(^{36})</td>
<td>PET-CT</td>
<td>41</td>
<td></td>
<td>CRG2: 3.7 (SD 1.9) (N = 11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CRG3: 3.6 (SD 2.3) (N = 18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CRG 4: 5.2 (SD 3.2) (N = 12)*</td>
</tr>
<tr>
<td>Dharmarajan (2012)(^{46})</td>
<td>PET-CT</td>
<td>94</td>
<td></td>
<td>7.0 (median) (0 to 31) (N = 58)</td>
</tr>
<tr>
<td>Eugene (2012)(^{38})</td>
<td>PET-CT</td>
<td>23</td>
<td>PET detected 17/18 tumours; CI detected 18/18; (4 sites were completely excised before imaging, 1 was not clearly identified at diagnosis)</td>
<td>6.2 (median) (2.7-15.4)</td>
</tr>
<tr>
<td>Federico (2012)(^{40})</td>
<td>PET-CT</td>
<td>30</td>
<td>PET detected all 21 tumours (8 completely excised before imaging; 1 unknown primary)</td>
<td>7.2 (2.5 to 19.2) (N = 18)</td>
</tr>
<tr>
<td>Klem (2007)(^{43})</td>
<td>PET</td>
<td>24</td>
<td>23 tumours evaluated (1 previously completely excised)</td>
<td>Initial staging: 7.7 (4.1 to 12.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1-13 days post-chemotherapy (first dose): 4.7 (2.4 to 8.4)</td>
</tr>
<tr>
<td>Ricard (2011)(^{15})</td>
<td>PET-CT</td>
<td>13</td>
<td>PET-CT detected 11/11 tumours including previously occult primary; CI detected 10/11. 2 patients had prior surgery; both PET and CI missed 1 microscopic residual lesion. Follow-up (N = 8) PET and CI both detected 3 residual local disease cases and 4 clear results. PET clear for 1 patient with positive CI; PET result confirmed true negative by follow-up.</td>
<td>Initial staging: 3.7 (median) (2 to 6.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Follow-up (N = 8) 5.8 (median) (5.2-6.1)</td>
</tr>
<tr>
<td>Tateishi (2009)(^{16})</td>
<td>PET-CT</td>
<td>35</td>
<td>Both PET-CT (using CT component) and CI correctly classified the T stage in all patients</td>
<td>NR</td>
</tr>
<tr>
<td>Volker (2007)(^{35})</td>
<td>PET</td>
<td>46 (11 RMS)</td>
<td>Both PET and CI detected all primary tumours</td>
<td>7.0 (SD 3.4)</td>
</tr>
</tbody>
</table>

CRG clinical risk group; SD standard deviation *all figures are mean SUV\(_{\text{max}}\)/SUV\(_{\text{liver}}\)