Rhabdomyosarcoma (RMS) is a rare cancer that primarily affects children and adolescents. Staging usually involves cross sectional imaging of the lesion, chest, abdomen and pelvis, a radiolabelled bone scan, and biopsies of the pelvic bone marrow.

Limited evidence suggests that PET / PET-CT has the potential to increase initial staging accuracy, specifically the detection of nodal involvement and distant metastatic spread.

The evidence is not sufficiently robust to determine whether PET-CT could replace one or more of the existing staging techniques.

Recommendations for research include the use of PET-CT in addition to standard staging techniques in an RCT of patients with RMS.

There is a need for good quality research into the value of other functional imaging techniques.
Background

Rhabdomyosarcoma (RMS) is a very rare cancer; the incidence is 4.6 per million children and adolescents under 20 years of age.\(^1,2\) The disease frequently presents as a soft-tissue mass, most commonly in the head and neck, the genitourinary tract, or the limbs.

In the UK treatment is delivered in designated centres and based on a multimodality approach including neoadjuvant chemotherapy, surgery, radiotherapy, and adjuvant chemotherapy. Overall outcomes have improved but remain suboptimal, with the 3 year event free survival rates for patients in Europe with localised disease of around 60%, and a corresponding overall survival of 80%.\(^3,4\)

Staging of patients with RMS is by cross-sectional imaging of the primary tumour, often with Magnetic Resonance Imaging (MRI), and further cross-sectional imaging of the chest, abdomen and pelvis. This is supplemented with a radiolabelled bone scan, and biopsies of the pelvic bone marrow.

Functional imaging techniques can demonstrate activity as well as the anatomical location of tumour masses.

The evidence

Six studies of PET-CT\(^7\)\(^\text{-}^{12}\) and two of PET\(^13,14\) reporting data on a total of 272 RMS patients were included in the review. No studies of DWI-MRI were identified. All eight included studies were retrospective opportunistic case series, an inherently weak study design, and most related to initial staging.

Survival and related outcomes

The only study reporting on overall survival found that the metabolic intensity of the primary tumour on PET had prognostic significance (\(p = 0.007\)).\(^7\) Also predictive of survival were PET detection of nodal involvement (\(p = 0.016\)), PET detection of metastases (\(p = 0.002\)) and a composite of the three (PET group; \(p = 0.002\)).

Three studies reported data on event-free survival.\(^7,12,15\) One found results which reflected those it reported for overall survival, with prognostic significance for primary tumour intensity (\(p = 0.005\)); lymph node detection (\(p = 0.008\)) and metastases detection (\(p = 0.01\)).\(^7\) A second study reported trends towards prognostic significance for PET-CT results using an alternative PET grading approach at initial staging (\(p = 0.08\)) and by PET positivity pre-radiation, after a median of 15 weeks chemotherapy (\(p = 0.06\)).\(^12\) At post-radiotherapy assessment PET-negative patients were significantly less likely to relapse than PET-positive individuals (\(p = 0.02\)). The third study, available as an abstract, reported no prognostic significance of PET at any point.\(^15\)

In a small subset of patients in one study, PET-CT was more likely to show complete response to treatment than conventional imaging; the majority of these patients were assessed by conventional imaging as having a partial response.\(^9\) All except one of these patients were in remission at follow-up.

PET-CT changed the management or treatment course of 7 out of 40 patients.\(^8,9,13\)

There were no data on acceptability. However three patient/relative representatives strongly supported the investigation of functional imaging; considering the burden of additional scans to be worthwhile if extra information could be gained.

Diagnostic data

The ability of functional imaging to detect primary tumours was good; only one known tumour site was missed and one previously occult primary was identified.

Patient level data from four studies indicated that PET-CT was better able to detect nodal involvement and individual positive nodes.

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Box 1. Functional imaging techniques evaluated

- **PET**, or positron emission tomography, involves the injection of a radio isotope that becomes concentrated in the area of interest and can be scanned as it decays to produce three dimensional images.

- **PET-CT** is a technique which combines PET with computed tomography (CT) in a single scan system to map the metabolic activity of tissues to the anatomical images.

- **Diffusion-weighted MRI (DWI-MRI)** is a magnetic resonance imaging scanning sequence that uses the microscopic mobility of water to map tissue architecture.

Nature of the evidence

This summary report is based on a systematic review commissioned by the Children’s Cancer and Leukaemia Group.\(^5\) The aim of the review was to see if there is evidence to support, or indicate potential for, the use of functional imaging either in addition to, or as a replacement for current imaging modalities at any stage of the treatment pathway; and to identify what, if any, further research is needed. Full methodological details are given in the CRD report.\(^6\)
than conventional imaging, with very few false positives (Table 1). Where reported, PET-CT also generated many fewer indeterminate results (1 versus 18) and more true negatives compared to conventional imaging. At the level of individual nodes one additional study found sensitivity and specificity for PET-CT to be 100% compared to 75% and 94% for conventional imaging.

These data also indicated that PET-CT was more likely to detect distant metastatic involvement than conventional imaging and produced fewer false positives (Table 1; Figure 1). At the level of individual lesions, one study reported better sensitivity and specificity for PET-CT (100% and 96%) compared to conventional imaging (66% and 91%).

### Conclusions

- Limited evidence suggests that PET / PET-CT has the potential to increase initial staging accuracy, specifically the detection of nodal involvement and distant metastatic spread.
- The evidence is not sufficiently robust to determine whether PET-CT could replace one or more of the existing staging techniques or whether it should be used in addition to them.
- There is little evidence as to the impact of PET-CT on assessment of therapeutic response or post-treatment assessment. There is also uncertainty as to the overall effect of using PET-CT on patient management and outcomes.
- DWI-MRI has not been sufficiently researched to answer questions of utility in imaging of childhood and adolescent RMS.

#### Recommendations for research

- All patients within an RCT cohort should be evaluated using PET-CT as an adjunct to conventional techniques at initial staging, treatment response and end of treatment.
- Interim and final analyses of the RCT data set should be used to identify where PET-CT could justifiably replace conventional staging techniques.
- The methodology of the PET-CT process should be standardised and fully reported.
- Results should be fully reported and individual patient data made available where possible.
- Any such study should assess the additional burden of treatment to the patient and healthcare system, assessing acceptability and prospectively evaluating resource use.
- There is a need for further comparative research on the role of DWI-MRI and other functional imaging techniques.

### Table 1. Patient level data

<table>
<thead>
<tr>
<th></th>
<th>PET-CT or PET</th>
<th>Conventional imaging</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Nodal involvement</td>
<td>80% (1 study)</td>
<td>89% to 100%</td>
</tr>
<tr>
<td></td>
<td>100% (3 studies)</td>
<td></td>
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<tr>
<td>Detection of distant metastatic sites</td>
<td>95% (1 study)</td>
<td>80% to 100%</td>
</tr>
<tr>
<td></td>
<td>100% (2 studies)</td>
<td></td>
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<tr>
<td></td>
<td>67% to 86%</td>
<td>90% or 100%</td>
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<tr>
<td></td>
<td>17% to 83%</td>
<td>43% to 100%</td>
</tr>
</tbody>
</table>

*Table 1. Patient level data*
References


This summary report is based on a systematic review commissioned by the Children’s Cancer and Leukaemia Group and undertaken by the Centre for Reviews and Dissemination (CRD). The full systematic review report examining the evidence for the use of functional imaging in the assessment of children and adolescents with Rhabdomyosarcoma, can be downloaded free of charge from the CRD website at: www.york.ac.uk/inst/crd/ or the Children’s Cancer and Leukaemia Group website at: www.cclg.org.uk. The views expressed in this summary report are those of the authors alone and not necessarily those of the Children’s Cancer and Leukaemia Group.

The Centre for Reviews and Dissemination is part of the NIHR and an academic department of the University of York. The centre undertakes systematic reviews evaluating the research evidence on health and public health questions of national and international importance. For further information go to www.york.ac.uk/inst/crd.