After about fourteen years of aggressive development by our group and others, active matrix flat-panel imagers (AMFPIs) have recently been commercially introduced to radiotherapy imaging. In this paper we report on the first comprehensive performance evaluation of a large area prototype AMFPI specifically developed for this application. This imager is based on an array of 512x512 pixels incorporating amorphous silicon photodiodes and thin-film transistors offering a 26x26 cm active area at a pixel pitch of 508 µm. The indirect detection array was coupled to various x-ray converters consisting of a phosphor screen (Lanex Fast B, Lanex Regular, or Lanex Fine) and a 1-mm-thick copper plate. Performance of the imager in terms of measured sensitivity, MTF, NPS and DQE is reported at beam energies of 6 and 15 MV and at doses of 1 and 2 MU. In addition, calculations of system performance (NPS, DQE) based on a cascaded-systems-formalism were performed and compared to empirical results. In these calculations, Swank noise and spatial energy distributions of secondary electrons were modeled by means of EGS4 Monte Carlo simulations. Results of measured system MTFs show a weak dependence on screen type (i.e, thickness), partially due to the presence of the secondary radiation spread. Measured DQE was found to be independent of dose for the Fast B screen implying that the imager is x-ray-quantum-limited at 1 MU, even at an extended source-to-detector distance of 200 cm. Finally, for this converter, good agreement between calculated and measured DQE was observed.