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Public Summary:
Positron emission tomography (PET) is a molecular imaging technique that can provide information on cellular functions in vivo. The PET imaging probe [\textit{18}F]-FDG is used clinically to detect, stage, and monitor cancer. Life-threatening acute liver failure can be triggered by a variety of factors, including common drugs such as Tylenol. PET imaging is rarely used to monitor liver diseases, in part due to a lack of specific imaging agents for liver function. PET imaging of the liver could have an important impact on the diagnosis and treatment of such conditions as acute liver failure and hepatocellular carcinoma. Here we report a new PET imaging probe, 2-deoxy-2-[\textit{18}F]fluororibose ([\textit{18}F]-2-DFR), for use in imaging liver function. We synthesized [\textit{18}F]-2-DFR from a carefully prepared molecular precursor, designed to withstand the harsh reaction conditions of late-stage fluorination. [\textit{18}F]-2-DFR accumulated preferentially in the mouse liver and was metabolized by enzymes that metabolize ribose. Notably [\textit{18}F]-2-DFR PET imaging could distinguish between healthy liver and liver damaged by acetaminophen. [\textit{18}F]-2-DFR is expected to be a useful PET probe for imaging and quantifying liver functions in vivo, with likely significant clinical utility.

Scientific Abstract:
Life-threatening acute liver failure can be triggered by a variety of factors, including common drugs such as acetaminophen. Positron emission tomography (PET) is rarely used to monitor liver function, in part because of a lack of specific imaging agents for liver function. Here we report a new PET probe, 2-deoxy-2-[\textit{18}F]fluororibose ([\textit{18}F]-2-DFR), for use in imaging liver function. [\textit{18}F]-2-DFR was synthesized and validated as a competitive substrate for the ribose salvage pathway. [\textit{18}F]-2-DFR was prepared through an efficient late stage radiofluorination. The desired selectivity of fluorination was achieved using an unorthodox protecting group on the precursor, which could withstand harsh SN2 reaction conditions with no side reactions. [\textit{18}F]-2-DFR accumulated preferentially in the liver and was metabolized by the same enzymes as ribose. [\textit{18}F]-2-DFR could distinguish between healthy liver and liver damaged by acetaminophen. [\textit{18}F]-2-DFR is expected to be a useful PET probe for imaging and quantifying liver functions in vivo, with likely significant clinical utility.

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