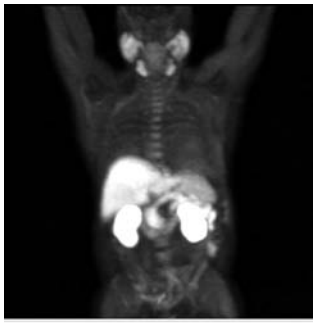
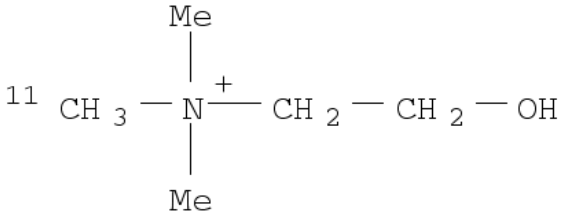
^{11}C-Choline

[^{11}C]choline chloride

SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

Radiopharmaceutical Name	^{11}C-choline chloride, [^{11}C]choline chloride Abbreviations: [^{11}C]CH	
Radiopharmaceutical Image Normal  Image provided by Dr. Val Lowe, Mayo Clinic	**Normal Biodistribution** After IV injection, ^{11}C-choline rapidly clears from the circulation (<3 min), with high clearance by liver and kidneys. Highest normal tissue uptakes are seen in renal cortex, liver, pancreas, salivary glands, variable bowel uptake, prostate, and pituitary gland. Low normal uptake is seen in cerebral cortex.	**Radiopharmaceutical Structure** 
Radionuclide	^{11}C Half-life 20.4 minutes	
Emission	Emission positron: Emax 0.970 MeV	
MICAD	http://www.ncbi.nlm.nih.gov/books/NBK23549/pdf/Choline11C.pdf	
Molecular Formula and Weight	^{11}C-choline chloride 139.62 g atom mole^{-1}	
General Tracer Class	Clinical Diagnostic PET Radiopharmaceutical	
Target	The target is neoplasms, particularly prostate cancer and brain tumors.	
Molecular Process Imaged	Various neoplasms have upregulated choline transport and phosphorylation. ^{11}C-choline is taken up by the tumors and phosphorylated by choline kinase to form phosphorylated ^{11}C-choline which is essentially trapped within cells. Slow metabolism to phospholipids also contributes to the signal, although the extent is minimal within the short time frame of the PET scan.	
Mechanism for in vivo retention	Metabolic trapping in the cell in the form of phosphorylated ^{11}C-choline	
Metabolism	Choline is phosphorylated by choline kinase and incorporated into various phospholipids in the body. In certain tissues, including kidney and liver, choline oxidation is prominent. The oxidative metabolite of choline is betaine. Betaine is excreted into the urine.	
Radiosynthesis	^{11}C-choline is synthesized by ^{11}C-methylation of dimethylethanolamine (DME) in acetone, followed by solid phase extraction isolation of the product from DME on a cation-exchange cartridge. The cartridge is rinsed with ethanol to remove residual DME before elution of the product with sterile saline through a sterilization filter.	
Availability	Due to the short half-life, it must be delivered within 2-3 half-lives from a producing cyclotron. Requires a site with an IND, NDA or ANDA filed with the Food and Drug Administration (FDA) for the radiopharmaceutical (IND = investigational new drug application, NDA = new drug application, ANDA = amended new drug application).	

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Status with USP / EuPh	An NDA was approved by the FDA in 2012 (NDA #203-155, Mayo Clinic). Status in US is the same as other PET radiopharmaceuticals (requires an IND, NDA or ANDA for use).
Recommended Activity and Allowable mass	**DOSAGE AND ADMINISTRATION** (Ref. Mayo Clinic NDA) IV administration, typically 370-740 MBq (10-20mCi) as a bolus.
Dosimetry	The effective dose (ED) is estimated to be 0.0040±0.0003 mSv/MBq (0.0148 rem/mCi) for adults. The dose-critical organ is the liver in adults, which receives 0.0131±0.0015 mGy/MBq (0.0485 rad/mCi) for adults.
Pharmacology and Toxicology	Pharmacokinetics: After intravenous injection, ^{11}C-choline is rapidly cleared from the blood stream ($T_{1/2}$ < 1 min). Distribution: ^{11}C-choline distributes mainly to the pancreas, kidneys, liver, spleen and colon. Based upon the relatively low urinary excretion of radioactivity, renal distribution is predominantly to the organ itself, rather than via formation of urine. Metabolism: Following intravenous administration, ^{11}C-choline undergoes metabolism resulting in the detection of ^{11}C-betaine as the major metabolite in blood. In a study of patients with prostate cancer or brain disorders, the fractional activities of ^{11}C-choline and ^{11}C-betaine in human arterial plasma appeared to reach a plateau within 25 minutes, with ^{11}C-betaine representing 82% ± 9% of the total ^{11}C detected at that time point. A small amount of unmetabolized 11C-choline was detected within the blood at the final sampling time point (40 minutes). Elimination: Urinary excretion of ^{11}C-choline was < 2% of the injected radioactivity at 1.5 hours after injection of the drug. The rate of ^{11}C-choline excretion in urine was 0.014 mL/min. Toxicology: Choline is a natural compound with no known toxic effects at levels present in the^{11}C-Choline injection. Long term studies have not been performed to evaluate the carcinogenic potential of ^{11}C-Choline.
Current Clinical Trials	The NIH clinical trials registry (www.clinicaltrials.gov) should be consulted for a list of current trials using ^{11}C-choline.
Reference Site / Person	The best reference at this time is Dr. Joseph Hung, Mayo Clinic. jhung@mayo.edu

Imaging Protocol	The imaging protocol for ^{11}C-choline can vary, but typically the procedure used is
	• On day before exam patient to drink 48 oz of water. On day of exam, 4 hr fast and drink 24 oz of water
	• 370-740 MBq (10-20mCi) as a bolus through a catheter inserted into a large peripheral vein.
	• Positioning of the patient on the imaging table:
	  • Patient supine, head first, head in head holder
	  • Arms elevated over the head for all procedures unless otherwise specified
	  • Metallic objects should be removed from the patient whenever possible
	• Scan Range:
	  • Routinely from ischial tuberosity to the base of skull, unless otherwise specified
	  • Make sure that the multiple CT reconstructions cover the same range
	• Scan direction for PET:
	  • Inferior to superior
	• Start imaging 2 minutes after the injection and acquire images for a total of 10-20 minutes in 2- or 3-D mode with 2–5 min per bed position depending on PET camera.

Human Imaging Experience	Listed below are selected references for ^{11}C-choline injection.

1. Tolvanen T, Yli-Kerttula T, Ujula T, Autio A, Lehikoinen P, Minn J, Roivinen A; Biodistribution and radiation dosimetry of [^{11}C] choline: a comparison between rat and human data. Eur J Nucl Med Mol Imaging. 2010; 37:874-83.

2. Scattoni V, Picchio M, Suardi N, Messa C, Freschi M, Roscigno M, Da Pozzo L, Bocciardi A, Rigatti P, Fazio F. Detection of lymph-node metastases with integrated [^{11}C]choline PET/CT in patients with PSA failure after radical retropubic prostatectomy: results confirmed by open pelvic retroperitoneal lymphadenectomy. Eur Urol. 2007; 52:423-9.

3. Rinnab L, Mottaghy FM, Simon J, Volkmer BG, de Petriconi R, Hautmann RE, Wittbrodt M, Egghart G, Moeller P, Blumstein N, Resks S, Kuefer R. [^{11}C]choline PET/CT for targeted salvage lymph node dissection in patients with biochemical recurrence after primary curative therapy for prostate cancer. Urologia Int. 2008; 81:191-7.

4. Reske SN, Blumstein NM, Glatting G. [^{11}C]choline PET/CT imaging in occult local relapse of prostate cancer after radical prostatectomy. Eur J Med Mol Imaging. 2008; 35:9-17.

5. Mitchell C, Kwon E, Lowe V, Hung J, Rangel L, Karnes RJ. Impact of ^{11}C-choline PET/CT scan on detection of recurrent prostate cancer in men with biochemical recurrence following failed initial treatment; supplemented with subject-level data. J Urol. 2012; 187:e823.

6. Mitchell C, Kwon E, Lowe V, Hung J, Rangel L, Karnes RJ. Detection of consolidated disease recurrences of prostate cancer by ^{11}C-choline PET/Scan: results confirmed by surgical resection; supplemented with subject-level data. J Urol. 2012; 187:e823.

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