Advisory Committee on Medical Uses of Isotopes (ACMUI)
Sub-Committee on Nursing Mother Guidelines for the Medical Administration of Radioactive Materials

Subcommittee Members:

Vasken Dilsizian, M.D., Darlene Metter, M.D. (Chair), Christopher Palestro, M.D.,

Pat Zanzonico, Ph.D.

Date: February 1, 2018
Revised: June 19, 2018
Final Report Submitted On: June 26, 2018

Introduction

Nursing or breast-feeding is the feeding of an infant from the female breast. Lactation is the process of milk production. Shortly after delivery and along with the initiation of supply and demand, the maintenance of lactation becomes relatively constant with a daily production of about 800 mL[1].

Milk production is influenced by many hormones, the most important being prolactin. The release of prolactin is dependent on the removal of milk from the breasts. Milk removal occurs with nursing and stimulates feedback mechanisms promoting the release of prolactin, and thus further milk production. When milk ceases to be removed from the breast, prolactin levels fall with a concomitant rise in "Feedback Inhibitor of Lactation," a protein which inhibits milk production. Complete cessation of milk production generally occurs about six weeks after the last breast-feeding.

At times, it is necessary to administer diagnostic or therapeutic radiopharmaceuticals to the nursing mother. Many of these agents appear in breast milk.[2] Therefore, the use of radiopharmaceuticals during nursing raises radiation exposure concerns for both the nursing infant and mother. For the nursing infant, this exposure comes internally, from the ingested radioactive milk, and externally, from exposure to the mother who is a radiation source in close proximity to the infant during nursing and child care. Consequently, the charge of this subcommittee is "To review the radiation exposure from diagnostic and therapeutic radiopharmaceuticals, including brachytherapy, to the nursing mother and child."

Current Guidance

Breast-feeding is not regulated. A nursing mother who has received unsealed byproduct material can be released by a licensee if the total effective dose equivalent to any other individual, including her nursing child, is projected to not exceed 5 mSv (0.5 rem). If a nursing mother continues to breast-feed after receiving a radiopharmaceutical and the nursing child's radiation exposure could exceed an effective dose equivalent of 1 mSv (0.1 rem), written instructions must be given to the mother regarding the potential adverse consequences if breast-feeding is not interrupted or ceased as well as guidance on the discontinuation of breast-feeding (10CFR 35.75)[3].

Radiation Safety

The ALARA (As Low As (is) Reasonably Achievable) principle is the Nuclear Regulatory Commission's (NRC) guidance on radiation safety (10 CFR 20.1003). ALARA directs the licensee and individuals to take every reasonable effort to decrease ionizing radiation exposure as far below regulatory dose limits as practically possible. These instructions should be individualized to include the consideration of available resources and their value in achieving this radiation exposure goal. Many nuclear medicine procedures are elective, and for the nursing mother it may be possible to delay these exams to allow for the interruption or, in some cases, the cessation of breast-feeding[4].

Before radioiodine therapy, oral and written radiation precaution instructions must be provided to the nursing mother and, as needed, to the appropriate family and/or caretakers. All patient, family or caretaker therapy concerns and questions should also be addressed. This information must be given in a sufficient individualized time frame to allow for appropriate radiation safety preparation, and should be provided at least six weeks prior to the anticipated radioiodine procedure, thereby allowing the necessary time for the cessation of lactation.

Radiopharmaceuticals

Radiopharmaceuticals consist of two components: the radioisotope and the non-radioactive carrier targeted for a specific molecule or metabolic pathway.

Once administered, these agents circulate and undergo both radioactive decay of the radioisotope and biologic elimination of the carrier component. The elimination half-time associated with the combined physical decay and pharmacokinetic clearance is termed the effective half-life.

The physical decay or half-life is the time required for a given quantity of radioactivity to decrease to one half of its original activity solely as a result of radioactive decay. For a radionuclide, ten physical half-lives will account for 99.999% of its radioactive decay[5].

The biological half-life is the time required to reduce the amount of a given substance in an internal organ or the whole body to one half of its original value solely as a result of biological elimination. Five biological half-lives of most drugs account for 97% of a drug's clearance, and presumably this clearance also applies to the radiopharmaceutical carrier component in breast milk[6].

Lactation and Breast-feeding Cessation

When a radiopharmaceutical is administered to a nursing mother who temporarily stops breast-feeding, it is advisable for her to breast pump during this "interruption period." The ongoing removal of breast milk from the breast will ensure that lactation will continue. Expression of milk will also facilitate the radiopharmaceutical's biologic elimination from the breast and therefore, an overall potential reduction in the radiation exposure to the maternal breasts.

During this interruption period, the mother may express and store her milk to be used after the milk is no longer radioactive, which is typically 10 physical half-lives of the radiopharmaceutical (i.e., ^{99m}Tc physical half-life is 6 hours, equating ten half-lives to 60 hours). Breast milk can also be expressed prior to radiopharmaceutical administration and used to feed the nursing child until breast-feeding can be resumed[7]. Alternatively, the nursing mother may choose to discard the expressed radioactive milk.

Nursing mothers should inform their healthcare provider of their breast-feeding status so that if a medical procedure involving radioactive material is contemplated, decisions can be made to maximize patient outcomes while minimizing the overall radiation risk to the nursing mother and infant[8].

Appropriate signage should also be posted in the nuclear medicine clinic/waiting room alerting women to notify the nuclear medicine staff before their procedure if they are breast-feeding.

Breast Milk and Drugs

When substances enter the maternal circulation, this vascular delivery allows for transfer of material from the glandular breast alveoli into maternal milk. Many factors control the regulation of this transfer and include the dramatic increase in blood flow to the lactating breast. Shortly after child delivery, a brief period of greater alveolar diffusion occurs which permits a higher level of antibodies, antibacterial factors and other substances to concentrate in breast milk. These diffusion factors are facilitated by low molecular weight, low protein binding and high lipid solubility of these substances[9].

Although the exact mechanism of radiopharmaceutical uptake into breast milk is unknown[10], a drug's concentration in the maternal circulation is generally proportional to its concentration in breast milk. In other words, higher serum levels generally result in a higher drug level in breast milk.

Radiopharmaceutical uptake by the breast is fairly rapid with peak concentrations at 3-4 hours after administration. It is of interest that studies on breast milk uptake have been highly variable for a given radiopharmaceutical and at different times within the same patient. The biological half-life however, appears less variable[11].

Radiation Exposure to the Maternal Lactating Breast from Diagnostic and Therapeutic Radiopharmaceuticals

Systemically administered radiopharmaceuticals will localize in variable amounts to all body tissues, including the breasts. In lactating breasts, enhanced uptake and secretion into breast milk may occur with certain radiopharmaceuticals and possibly their radioactive metabolites[12 13 14 15 16 17 18 19 20 21 22 23 24]. This greater uptake would result in an increased radiation dose to the lactating relative to the non-lactating breast. Due to the relatively high sensitivity of the female breast to radiation carcinogenesis[25], the enhanced radiation dose to the lactating breast warrants consideration. This section therefore addresses the radiation dose to lactating breasts and provides absorbed dose estimates for commonly used radiopharmaceuticals (Table 1).

The time-integrated activity (also known as the cumulated activity or residence time) in the lactating breast results from radiopharmaceutical secretion into breast milk and was estimated by Stabin and Breitz[26]. These investigators assumed a linear filling of milk into the breast to a milk volume of 142 ml over 4 hours and then instantaneous emptying at feeding or pumping. The breast absorbed dose was calculated by using the breast-to-breast S values for the Reference Adult female anatomic model of Stabin et al[27]. No attempt was made to model the effect of a temporary interruption of breast-feeding since the mother would likely express/pump milk from her breasts at regular intervals, and the net effect would be comparable to actual breast-feeding.

The 2- to 5-fold increase in breast mass that occurs during pregnancy and lactation was also considered. Due to individual variability, these changes were difficult to model with certainty. However, the overall effect of a larger lactating breast would be a decrease in the absorbed breast dose, since the radioactivity will be deposited over a larger mass. Stabin and Breitz used a standard breast mass (400 g for both breasts) which produced a conservative upper-limit breast dose estimate for most women and a reasonable though less conservative estimate for smaller breasts.

For ^{18}F-FDG, the individual breast activity, expressed as the standard uptake value (SUV), was measured by Hicks et al[28] in a series of oncology patients at one hour after ^{18}F-FDG injection. Since the biokinetics of FDG are well known, the one-hour SUV was assumed to reflect the maximum breast activity. Conservatively, the kinetics of FDG breast uptake were ignored (i.e., uptake was considered instantaneous) and elimination of activity was assumed to occur only by physical decay (i.e., ignoring the effect of actual breast feeding or pumping). Given the short physical half-life of ^{18}F (1.2 hours), the latter assumption is likely not overly conservative. The ^{18}F-FDG breast-to breast absorbed dose was calculated using the *OLINDA* computer program[29],

again assuming breast-to-breast S values for the Reference Adult Female model[30]. The absorbed-dose estimates for the lactating breast thus corresponds to self-irradiation (i.e., breast-to-breast) values.

For the majority of radiopharmaceuticals, once in the maternal circulation, there is less than 10% excretion into breast milk, with most estimates at 0.3 to 5% of the administered activity[31]. Several authors have reported higher radiopharmaceutical concentrations and cumulative excretions in patients with greater milk production. Cumulative excretions greater than 10% have been reported only for ^{67}Ga-citrate and ^{131}I-NaI [32]. Consequently, except for ^{67}Ga-citrate and ^{131}I-NaI, the highest absorbed dose estimates to the lactating breasts for typical diagnostic administered activities are usually well under 1 rad (0.01 Gy). ^{67}Ga-citrate and ^{131}I-NaI are both actively secreted into breast milk, and result in notably higher absorbed doses to the lactating breast: 1.1 rad (0.011 Gy) for an administered activity of 5 mCi (185 MBq) of ^{67}Ga-citrate and 200 rad (2 Gy) for a therapeutic administered activity of 150 mCi (5,550 MBq) of ^{131}I-NaI. The exceptionally high ^{131}I-NaI dose to the lactating breasts is worrisome, and has led to recommendations for lactating women for whom radioiodine therapy is planned to discontinue breast-feeding six weeks prior to therapy[33] [34]. This recommendation ensures the complete cessation of lactation, which minimizes radioiodine concentration in the maternal breast, and thus, the absorbed maternal breast dose.

Radiation Exposure: Nursing Child from Nursing Mother

The physical and other relevant properties of the radionuclides considered in the following dosimetric analyses are provided in Table 2.

(a) External Maternal Radiation to the Nursing Child

The most obvious mode of radiation exposure to a nursing child from radiopharmaceutical administration to the child's mother is ingestion of radioactive maternal milk. In addition, the nursing child will be exposed externally from radioactivity in the mother, and this exposure may be significant given the close proximity of the mother and child during nursing and child care. Given the general lack of pertinent data in the literature, the external absorbed dose to the nursing child has been estimated by the following model calculations:

$$D_{\text{nursing child}}\big|_{\text{ext}} = D_{\text{nursing child}\leftarrow\text{maternal breast}}\big|_{\text{ext}} + D_{\text{nursing child}\leftarrow\text{maternal rem}}\big|_{\text{ext}} \quad (1)$$

where

$D_{\text{nursing child}\leftarrow\text{maternal breast}}\big|_{\text{ext}}$ = the external absorbed dose to the nursing child from activity in the maternal breast

and

$D_{\text{nursing child}\leftarrow\text{maternal rem}|\text{ext}}$ = the external absorbed dose to the nursing child from activity in the maternal remainder of body (assumed to be equivalent to the maternal torso).

The external absorbed dose to the nursing child from activity in the maternal breast, $D_{\text{nursing child}\leftarrow\text{maternal breast}|\text{ext}}$, and in theremainder of the mother's body, $D_{\text{nursing child}\leftarrow\text{maternal rem}|\text{ext}}$, can be calculated by Equations (2) and (3), respectively:

$$D_{\text{nursing child}\leftarrow\text{maternal breast}|\text{ext}} = \tau_{\text{maternal breast}} \bullet A \bullet \Gamma \bullet \frac{1}{r_{\text{breast-to-child}}^2} \bullet CF_{\text{point-to-line}|\text{breast}} \bullet 0.5 \bullet [1-\phi(\text{breast-to-breast})] \bullet E_{\text{nursing}} \quad (2)$$

and

$$D_{\text{nursing child}\leftarrow\text{maternal rem}|\text{ext}} = \tau_{\text{maternal rem}} \bullet A \bullet \Gamma \bullet \frac{1}{r_{\text{maternal rem-to-child}}^2} \bullet CF_{\text{point-to-line}|\text{maternal rem}} \bullet 0.5 \bullet [1-\phi(\text{maternal WB}\leftarrow\text{maternal WB})] \bullet E_{\text{nursing}} \quad (3)$$

where $\tau_{\text{maternal breast}}$ = the radionuclide residence time in the maternal breast (in h),

$\tau_{\text{maternal rem}}$ = the radionuclide residence time in the maternal remainder of body (in h),

A = the administered activity (in μCi),

Γ = the radionuclide specific gamma-ray constant (in R-cm^2/μCi-h) [35],

$r_{\text{breast-to-child}}$ = the maternal breast-to-child distance (in cm), that is, the distance from the mid-line of the maternal breast to the mid-line of the nursing child

= 7.5 cm [36]

$r_{\text{maternal rem-to-child}}$ = the maternal remainder of body-to-child distance (in cm), that is, the distance from the mid-line of the mother's torso to the mid-line of the nursing child

= 15 cm [37]

$CF_{\text{point-to-line}|\text{breast}}$ = the point source-to-line source conversion factor for the breast

= 0.32 [38]

$CF_{\text{point-to-line}|\text{maternal rem}}$ = the point source-to-line source conversion factor for the maternal remainder of body (corresponding to the maternal torso),

ϕ(breast-to-breast) = the breast-to-breast photon absorbed fraction

$= 0.54$ [39]

ϕ(maternal WB-to-maternal WB)

= the maternal whole body (WB)-to-maternal whole body (WB) photon absorbed fraction,

and $E_{nursing}$ = the occupancy factor for nursing

$= 0.33$ [40]

The radionuclide residence times in the breast milk, $\tau_{maternal\ breast}$, and in the maternal remainder of body, $\tau_{maternal\ rem}$, can be calculated by Equations (4) and (5), respectively:

$$\tau_{breast\ milk} = 1.44 \bullet f_{breast\ milk} \bullet \sum_{i=1}^{n} f_i|_{breast\ milk} \bullet (T_e)_i|_{breast\ milk} \quad (4)$$

and

$$\tau_{maternal\ rem} = 1.44 \bullet F_{maternal\ rem} \bullet \sum_{i=1}^{n} f_i|_{maternal\ rem} \bullet (T_e)_i|_{maternal\ rem} \quad (5)$$

where $f_{breast\ milk}$ = the fraction of the administered activity in breast milk,

$f_i|_{breast\ milk}$ = the fraction corresponding to component i of the exponential function describing the time-activity data for breast milk,

$(T_e)_i|_{breast\ milk}$ = the effective half-time of component i of the exponential function describing the time-activity data for breast milk (conservatively equated with the physical half-life of the radionuclide, T_p, if a literature value of biological half-time of the particular radiopharmaceutical is not available),

$$= [T_p \bullet (T_b)_i|_{breast\ milk}] / [T_p + (T_b)_i|_{breast\ milk}] \quad (6)$$

$(T_b)_i|_{breast\ milk}$ = the biological half-time of component i of the exponential function describing the time-activity data for breast milk,

$f_{maternal\ rem}$ = the fraction of the administered activity in maternal remainder of body,

$f_i|_{maternal\ rem}$ = the fraction corresponding to component i of the exponential function describing the time-activity data for the maternal remainder of body,

and $(T_e)_i|_{maternal\ rem}$ = the effective half-time of component i of the exponential function describing the time-activity data for the maternal remainder of body (conservatively equated with the physical

half-life of the radionuclide, T_p, if a literature value of biological half-time of the particular radiopharmaceutical is not available)

$$= [T_p \bullet (T_b)_i|_{\text{maternal rem}}] / [T_p + (T_b)_i|_{\text{maternal rem}}] \quad (7)$$

$(T_b)_i|_{\text{maternal rem}}$ = the biological half-time of component i of the exponential function describing the time-activity data for the maternal remainder of body.

Implicit in equations (2) and (3) is the assumption that the beta-particle contribution to the external dose from the mother to the nursing child is negligible; given the very short range of beta particles in tissue, this is a reasonable assumption. The factor, 0.5, in Equations (2) and (3) reflects the fact that radiations emitted from within the mother have an equal probability of traveling either towards or away from the nursing child. Furthermore, rather than modeling the maternal breast and torso as point sources, they have been modeled as line sources as described by Siegel et al[41]. This provides a more accurate approach to estimating the distance-dependence of the mother-to-child doses than the conventional point-source model.

(b) Internal Radiation Dose to the Nursing Child from Ingestion of Radioactive Milk

The second major pathway of radiation exposure to a nursing child resulting from radiopharmaceutical administration to the child's mother is the ingestion of radioactive maternal milk. As already noted, generally less than 10% of an administered radiopharmaceutical activity is excreted into breast milk; typical estimates range from 0.3% to 5% of the initial administered activity[42]. Higher cumulative excretions been reported only with ^{67}Ga-citrate and ^{131}I-NaI up to ~10 and ~25%, respectively[43]. Based on the maximum fraction of the administered activity in breast milk (/ml) and the half-time(s) of clearance from breast milk in Table 3 and assuming breast-milk volumes of 142 mL (Stabin and Breitz[26]) , radiopharmaceutical residence times can be calculated using equation (4).

Assuming complete ingestion of the 142 mL (Stabin and Breitz[26]) of radioactive milk by the nursing child and ignoring the subsequent kinetics of absorption and clearance from the child, the whole-body residence time of the radiopharmaceutical in the child can be equated with its residence time in the breast milk, $\tau_{\text{breast milk}}$. An upper limit of the whole-body absorbed dose to the nursing child (specifically, for the Reference Newborn anatomic model) from ingestion of radioactive milk, $D_{\text{nursing child}}|_{\text{int}}$, can then be derived using equation (8):

$$D_{\text{nursing child}}\big|_{\text{int}} = \tau_{\text{breast milk}} \bullet DF(WB \leftarrow WB)_{\text{newborn}} \quad (8)$$

where

$DF(WB \leftarrow WB)_{newborn}$ = the whole body-to-whole body dose factor (in rad/uCi-h) for the Reference Newborn anatomic model.

Radioiodine is avidly concentrated by the thyroid, achieving decay-corrected uptakes at 24 hours post-administration of ~60% in euthyroid newborns [44] and delivering uniquely high doses to the thyroid. For ^{123}I-, ^{124}I-, and ^{131}I-iodide, therefore, the residence times in the newborn thyroid (assuming a 60% thyroid uptake and an effective half-life calculated using a thyroid biological half-life of 60 d [45] and the physical half-life of the particular radioiodine) as well as whole-body ($\tau_{nursing\ child|thyroid}$ and $\tau_{breast\ milk}$, respectively) were calculated and the thyroid-to-thyroid and thyroid-to-whole body ($D_{nursing\ child|thyroid\text{-}to\text{-}thyroid}$ and $D_{nursing\ child|thyroid\text{-}to\text{-}WB}$, respectively) as well as whole-body-to-whole absorbed doses ($D_{nursing\ child|int}$) were calculated using equations (9) and (10):

$$D_{nursing\ child|thyroid\text{-}to\text{-}thyroid} = \tau_{nursing\ child|thyroid} \bullet DF(thyroid \leftarrow thyroid)_{newborn} \quad (9)$$

and $$D_{nursing\ child|thyroid\text{-}to\text{-}WB} = \tau_{nursing\ child|thyroid} \bullet DF(thyroid \leftarrow WB)_{newborn} \quad (10)$$

where $DF(thyroid \leftarrow thyroid)_{newborn}$ = the thyroid-to-thyroid dose factor (in rad/uCi-h) for the Reference Newborn anatomic model

and $DF(thyroid \leftarrow WB)_{newborn}$ = the thyroid-to-whole body dose factor (in rad/uCi-h) for the Reference Newborn anatomic model.

All dose factors (DF) were taken from Stabin MG, Sparks RB, and Crowe E. OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med. 46:1023-7, 2005.

(c) Total Radiation Dose to the Nursing Child

The total radiation dose to a nursing child per feeding for various radiopharmaceuticals administered to the nursing mother were calculated by summing the respective external and internal radiation doses. The dose contributions to the nursing newborn were calculated for each feeding, assuming 142 ml of radioactive breast milk ingested every 4 hours (Stabin and Breitz[26]). The dose contributions per feeding were then summed to yield the total cumulative dose to the limiting tissue, either the whole body or, in the case of radioiodides, the thyroid, of a nursing newborn (Table 3). Note that the dose estimates in Table 3 are for the specific administered activities in the table. If breast-feeding were *not* discontinued, the doses to the newborn tissues (whole body or thyroid) would uniformly exceed 0.1 rad (= 100 mrad). This 0.1-rad value is widely used as the dose limit in formulating guidelines for the discontinuation of breast-feeding by nursing mothers undergoing nuclear medicine procedures. The 0.1-rad value to the whole body of a nursing newborn would not be exceeded, for ^{68}Ga-octreotate, ^{82Rb}-chloride and ^{123}I-MIBG even if breast-feeding were *not* discontinued. For ^{18}F-FDG and ^{99m}Tc-labeled

radiopharmaceuticals, only relatively brief interruptions of breast-feeding (a few hours to ~1 day) are needed to comply with the 0.1-rad dose value.

However, ^{67}Ga-citrate, ^{111}In-OCTREOTATE, ^{111}In-labelled white blood cells, ^{124}I-NaI, ^{131}I-NaI, ^{131}I-MIBG, and ^{177}Lu-octreotate (therapy) doses to the limiting newborn tissues (whole body or thyroid), exceed the 0.1-rad value by more than one to several orders of magnitude. The durations of discontinuation of breast-feeding to achieve a dose of 0.5 rad as well as 0.1 rad to the limiting newborn tissues (whole body or thyroid) are presented in Table 4. For ^{67}Ga-citrate, ^{111}In-OCTREOTATE, ^{111}In, white blood cells, ^{124}I-NaI, ^{131}I-NaI, ^{131}I-MIBG, and ^{177}Lu-octreotate (diagnosis and therapy), discontinuation of breast-feeding for several weeks to a month is required to achieve a whole-body or thyroid dose to the nursing newborn of 0.1 rad or even 0.5 rad.

The magnitude of the radiation dose to the nursing child for ^{131}I-NaI, especially for therapy, reinforces the need for permanent discontinuation of breast-feeding for the current child following ^{131}I-NaI administration to the nursing mother. Breast feeding, however, is allowed for future pregnancies. The radiation dose to the nursing child's thyroid is considerably higher than that to the whole-body (with the potential for damage to the child's thyroid), further reinforcing the need to cease breast-feeding for any ^{131}I-NaI administration.

For ^{67}Ga-citrate, the dose to the nursing mother's breast and the whole-body dose to the nursing child will be significant as well if breast-feeding is not discontinued (see Tables 3 and 4). However, based on the dose estimates to the maternal breast (Table 1), and in contrast to the recommendation for a therapeutic administration of ^{131}I-NaI discontinuation of breast-feeding *prior* to the administration of ^{67}Ga-citrate is not required. Following administration of ^{67}Ga-citrate, discontinuation of breast-feeding for a period of 4 weeks is recommended, which is consistent with the most conservative recommendation in the literature.

Radiation Exposure to the Nursing Child from Implanted Sources: Brachytherapy and Radioactive Seed Localization

Brachytherapy is used to treat breast cancer, especially in breast conservation surgery for early-stage cancer[46] [47] [48]. The purpose of brachytherapy is to deliver a localized boost dose to the lumpectomy bed after whole-breast radiation. Several brachytherapy treatments are usually required. After each treatment, the radioactive seed is removed and no radioactivity remains in the breast. Accordingly, except for suspending breast-feeding while the sources are in place, brachytherapy does not present any restrictions on breast-feeding.

Radioembolic therapy using ytrrium-90 (^{90}Y)-labeled microspheres (SirSpheres™, TheraSperes™) is used for treating unresectable liver tumors[49] [50]. Under fluoroscopic guidance the radiolabeled microspheres are infused intra-arterially to selectively treat tumors, thereby relatively sparing normal tissue. The ^{90}Y microsphere system is considered a medical device (i.e., a brachytherapy device) and is licensed under 10CFR35.1000 ("Other medical uses of

byproduct material or radiation from byproduct material"). As a pure beta emitter, ^{90}Y does not cause a significant external radiation hazard from the resulting *bremsstrahlung*, which produces only a negligible external dose[51]. For lactating mothers who receive ^{90}Y -microspheres breast-feeding does not need to be interrupted, as the ^{90}Y does not enter the systemic circulation, breast tissue or breast milk. As noted, there is no significant external dose to the child (as only the potential source of external radiation from ^{90}Y is the very low-yield emission of *bremsstrahlung*).

The purpose of radioactive seed localization (RSL) is to preoperatively localize suspicious non-palpable breast lesions for surgical excision[52] [53]. RSL is an alternative to the traditional needle-wire preoperative localization, wherein a non-radioactive percutaneous wire is placed into the breast to guide surgical excision of suspicious tissue.

The RSL seed(s) may be removed intra-operatively from the tissue specimen or more commonly, the tissue specimen containing the seed(s) is sent to Pathology for seed removal, analysis and documentation. Breast-feeding should be suspended while the seeds are in place. No radioactivity remains in the breast once all seeds have been removed and accounted for. Breast-feeding can be continued up to seed implantation and resumed immediately after seed removal.

Precautions for Nursing Mothers: Recommendations and Rationale

Existing recommendations for nursing mothers promulgated by the NRC[54], the International Commission on Radiological Protection (ICRP)[55], and others[56] are based on a maximum dose (i.e., dose equivalent) to the nursing child of 0.1 rad. The extant recommended precautions for nursing mothers, summarized in Table 5, are somewhat variable in terms of both the radiopharmaceuticals included and the time interval for breast feeding interruption following radiopharmaceutical administration to the nursing mother.

In formulating the current recommendations (tabulated below), our Sub-Committee has adopted the 0.1-rad dose limit to the whole body or, in the case of radioiodides, the thyroid. To the extent that it is practical, expressed radioactive milk can be held for decay in storage for the same length of time as the recommended interruption period and then used for feeding the child. The Sub-Committee's recommended interruption periods apply not only to breast-feeding but also to the close physical proximity of the nursing mother to the nursing child (i.e., caressing or holding the child with a similar distance to the mother as for breast-feeding).

Specific Sub-Committee recommendations for the nursing mother include the following:

1. For ^{99m}Tc-labeled radiopharmaceuticals, rather than a radiopharmaceutical-specific interruption period, a single 24-hour interruption period is recommended. Although this time interval may be longer than necessary for some ^{99m}Tc-labeled radiopharmaceuticals, it is compliant with the 0.1-rad dose limit and simplifies the guidance, thereby avoiding confusion and reducing the likelihood of error.

2. For ^{18}F-FDG and ^{68}Ga-OCTREOTATE, a 4-hour discontinuation period is recommended. This recommendation (especially conservative for ^{68}Ga-OCTREOTATE) is cautious and simplifies safety instructions for patients and medical professionals.

3. For very-short-lived positron-emitting radionuclides used in imaging, carbon-11 (^{11}C) (physical half-life: 20.4 min), nitrogen-13 (^{13}N) (9.97 min), and oxygen-15 (^{15}O) (2.04 min), and generator-produced rubidium-82 (^{82}Rb) (1.27 min), no interruption in breast-feeding is recommended, since there is no significant activity remaining in the mother by the time of the next feeding.

4. For iodine-123 in the form of NaI (^{123}I-NaI), a discontinuation period of 3 days is recommended. This is in marked contrast to the past, where complete cessation of breast-feeding for the current child was recommended. This prior ^{123}I-NaI recommendation was based on contamination (up to 2.5% of the total activity) with long-lived iodine-125 (^{125}I) (physical half-life: 60 days) that occurred with older methods of ^{123}I production[57]. Such contamination of ^{123}I with ^{125}I no longer occurs. T herefore, the restrictions on breast-feeding following ^{123}I-NaI administration to the nursing mother may be justifiably relaxed to a discontinuation period of 3 days.

5. For iodine-124 and iodine-131in the form of iodide (^{124}I- and ^{131}I-NaI), breast-feeding should be discontinued permanently for the current child - even for diagnostic administrations – due to the very high doses to the child's thyroid. Breast feeding should also be discontinued 6 weeks prior to *therapeutic* radioiodine administration to cease lactation which will decrease the radiation dose to the maternal breast.

6. For gallium-67 (^{67}Ga)-gallium-citrate, an interruption period of 28 days is recommended, which is consistent with the most conservative recommendations for ^{67}Ga in the literature. For indium-111 (^{111}In)-labeled white cells and OCTREOTATE an interruption period of 6 days and for thallium-201 (^{201}Tl-chloride) an interruption period of 4 days are recommended.

7. For zirconium-89 (^{89}Zr), a 28-day (i.e., 4-week) interruption period was set equal to the maximum recommended interruption period for ^{67}Ga. The rationale for this recommendation are the comparable physical half-lives of ^{89}Zr (3.27 days) and ^{67}Ga (3.26 days), both ^{89}Zr and ^{67}Ga are radiometals and may share some common chemical properties, and lastly, there is a lack of relevant data on ^{89}Zr-labeled agents in nursing mothers.

   Perhaps somewhat surprisingly, for *therapeutic* lutecium-177 (^{177}Lu)-OCTREOTATE (211-mCi administered activity), a discontinuation period of ~28 days (i.e., 4 weeks) appears adequate. For diagnostic ^{177}Lu-OCTREOTATE (50 mCi), a discontinuation period of ~19 days should suffice. Out of an abundance of caution, however, permanent discontinuation of breast-feeding for the current child is recommended following either therapeutic or diagnostic ^{177}Lu-OCTREOTATE administration. (The unusually high diagnostic activity of ^{177}Lu-OCTREOTATE, 50 mCi, is necessitated by the low yield (only ~10%) of imageable photons emitted by ^{177}Lu.)

8. For radium-223 (^{223}Ra) and all other alpha particle-emitting radionuclides, permanent discontinuation of breast-feeding for the current child is recommended. Alpha particles are densely ionizing, have high-linear energy transfer (LET) radiations that potentially incur far more significant biological effects than beta-particles, and are of particular concern in the young child in whom rapid growth and development are occurring. In the absence of relevant data and out of an abundance of caution, permanent discontinuation of breast-feeding for the current child is therefore recommended.

Subcommittee Recommendations for the Nursing Mother

Radiopharmaceutical	**Breast-feeding Discontinuation to Achieve 0.1 rad to the Limiting Tissue**
^{15}O, ^{82}Rb	No discontinuation
^{11}C, ^{13}N	1 hour
^{18}F	4 hours
^{68}Ga	4 hours
^{99m}Tc	24-hours
^{123}I-NaI	3 days
^{111}In-white blood cells, -OCTREOTATE	6 days
^{201}Tl-chloride	4 days
^{67}Ga and ^{89}Zr	28 days
^{124}I-NaI	Stop breast feeding
^{131}I-NaI	Stop breast feeding
^{177}Lu-OCTREOTATE - diagnostic or therapeutic	Stop breast feeding
^{223}Ra and all alpha emitters	Stop breast feeding

Patient Information: Departmental Signage for Nursing Mothers

Nursing mothers undergoing a nuclear medicine or nuclear cardiology procedure may not be aware of the potential dosimetric impact of such procedures on themselves and their nursing child. It is important that nuclear medicine and nuclear cardiology facilities therefore alert nursing mothers that certain radiation safety precautions with respect to breast-feeding may be required before and after they receive a radiopharmaceutical. Analogous to the posting or signage used to alert pregnant and potentially pregnant patients to possible hazards of nuclear medicine and radiological procedures, the following or equivalent should be prominently displayed in all patient areas of a nuclear medicine or nuclear cardiology facility: "If you are currently breast-feeding or plan to begin breast-feeding in the near future, inform the technologist, nurse or doctor immediately." Depending on the patient demographics in a particular facility, posting such signage in various foreign languages as well as in English should be considered.

Table 1

Radiopharmaceutical Absorbed Doses to the Lactating Breast

			Breast Absorbed Dose[58 59]			
	Administered Activity		Lowest Estimate		Highest Estimate	
Radiopharmaceutical	mCi	MBq	Rad	Gy	rad	Gy
^{18}F-FDG	10	370	1.2E-01	1.2E-03	2.0E-01	2.0E-03
^{51}Cr-EDTA	0.05	1.85	4.2E-07	4.2E-09	2.5E-06	2.5E-08
^{67}Ga-citrate	5	185	2.2E-02	2.2E-04	1.1E+00	1.1E-02
^{99m}Tc-DTPA	20	740	6.1E-04	6.1E-06	1.2E-02	1.2E-04
^{99m}Tc-DTPA aerosol	1	37	1.2E-05	1.2E-07	2.5E-04	2.5E-06
^{99m}Tc-DISIDA	8	296	2.0E-03	2.0E-05	6.0E-03	6.0E-05
^{99m}Tc-glucoheptonate	20	740	3.6E-03	3.6E-05	7.4E-03	7.4E-05
^{99m}Tc-HAM	8	296	8.5E-03	8.5E-05	2.3E-02	2.3E-04
^{99m}Tc-MAG3	5	185	3.0E-04	3.0E-06	6.0E-03	6.0E-05
^{99m}Tc-MAA	4	148	1.6E-03	1.6E-05	1.2E-01	1.2E-03
^{99m}Tc-MDP	20	740	2.7E-03	2.7E-05	3.8E-03	3.8E-05
^{99m}Tc-MIBI	30	1110	5.5E-04	5.5E-06	5.1E-03	5.1E-05
^{99m}Tc-PYP	20	740	4.2E-03	4.2E-05	2.2E-02	2.2E-04

^{99m}Tc-RBCs - in vitro labeling	20	740	9.3E-04	9.3E-06	1.6E-03	1.6E-05
^{99m}Tc-RBCs - in vivo labeling	20	740	2.5E-04	2.5E-06	1.1E-01	1.1E-03
^{99m}Tc-pertechnetate	30	1110	1.9E-03	1.9E-05	2.5E-01	2.5E-03
^{99m}Tc-sulfur colloid	12	444	3.2E-03	3.2E-05	4.6E-02	4.6E-04
^{99m}Tc-WBCs	10	370	1.1E-02	1.1E-04	1.5E+00	1.5E-02
^{111}In-WBCs	0.5	18.5	5.0E-04	5.0E-06	2.5E-03	2.5E-05
^{123}I-MIBG	10	370	-	-	2.7E-02	2.7E-04
^{123}I-NaI	0.4	15	-	-	4.7E-02	4.7E-04
^{123}I-OIH	2	74	5.5E-03	5.5E-05	5.8E-02	5.8E-04
^{125}I-OIH	0.01	0.37	-	-	8.5E-05	8.5E-07
^{131}I-OIH	0.3	11	5.0E-03	5.0E-05	3.2E-02	3.2E-04
^{131}I-NaI [a]	150	5,550	-	-	2.0E+02	2.0E+00
^{201}Tl-chloride	3	111	2.4E-03	2.4E-05	4.1E-03	4.1E-05

[a] The radiation dose to the lactating breast for ^{124}I-NaI is likely comparable to that for ^{131}I-NaI.

Table 2

Physical Properties of Radionuclides Relevant to Nursing Mother Guidelines [a] (60)

Radionuclide	Physical Half-Life, T_p (h)	Principal Gamma- and X-ray Energies (keV)	Specific Gamma-Ray Constant, Γ (R-cm2/uCi-h)	Absorbed Fractions (Gamma- and X-rays) ϕ(maternal WB←maternal WB)	ϕ(Br←Br)	Dose Factors (rad/uCi-h) DF(WB←WB)$_{newborn}$	DF(thyroid←thyroid)$_{newborn}$	DF(thyroid←WB)$_{newborn}$
Carbon-11 (^{11}C)	0.333	511	0.00586	0.313	0	0.000332	not applicable	not applicable
Oxygen-15 (^{15}O)	0.0339	511	0.00586	0.313	0	0.000539	not applicable	not applicable
Nitrogen-13 (^{13}N)	0.166	511	0.00586	0.313	0	0.000396	not applicable	not applicable
Fluorine-18 (^{18}F)	1.83	511	0.00568	0.313	0	0.000244	not applicable	not applicable
Gallium-67 (^{67}Ga)	78.2	93, 185, 300	0.000803	0.329	0	0.0000365	not applicable	not applicable
Gallium-68 (^{68}Ga)	1.13	511	0.00543	0.313	0	0.000535	not applicable	not applicable
Rubidium-82 (^{82}Rb)	0.0212	511	0.00633	0.313	0	0.000396	not applicable	not applicable
Zirconium-89 (^{89}Zr)	78.4	511	0.00659	not applicable	0	not applicable	not applicable	not applicable
Technetium-99m (^{99m}Tc)	6.04	140	0.000795	0.330	0	0.0000216	not applicable	not applicable
Indium-111 (^{111}In)	67.3	173, 245	0.00346	0.313	0	0.0000650	not applicable	not applicable
Iodine-123 (^{123}I)	13.1	159	0.00143	0.330	0	0.0000394	5.02E-02	4.44E-05
Iodine-124 (^{124}I)	100.2	511	0.00659	0.313	0	0.000229	3.16E-01	2.50E-04
Iodine-131 (^{131}I)	193.0	364	0.00220	0.313	0	0.000153	3.26E-01	1.60E-04
Lutetium-177 (^{177}Lu)	159.5	137, 208	0.000181	0.313	0	0.0000908	not applicable	not applicable
Thallium-201 (^{201}Tl)	72.9	69-80, 167	0.000450	0.346	0	0.0000299	not applicable	not applicable
Radium-223 (^{223}Ra)	274.3	45, 55, 81,84, 270	0.000770	not applicable	0	not applicable	not applicable	not applicable

[a] The physical half-lives and gamma- and x-ray energies are taken from Eckerman K and Endo A. MIRD Radionuclide Data and Decay Schemes, 2nd ed. Society of Nuclear Medicine, Reston, VA, 2007. The specific gamma-ray constants are taken from Smith DS and Stabin MG. Exposure rate constants and lead shielding values for over 1,100 radionuclides. Health Phys 102: 271-291, 2012. The absorbed fractions are taken from Cristy M and Eckerman KF. Specific Absorbed Fractions of Energy at Various Ages from Internal Sources. V. Fifteen-Year-Old Male and Adult female, ORNL/TM-8381/V5, Oak Ridge National Laboratory, Oak Ridge, TN, 1987. The dose factors (also known as S values) are taken from Stabin MG, Sparks RB, and Crowe E: OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med. 46:1023-7, 2005.

[b] The maternal breast-to-maternal breast absorbed fractions, ϕ(Br←Br) for gamma- and x-rays were uniformly set to 0. This is a conservative assumption in that it maximizes the estimated external absorb dose to the nursing baby in that ϕ(Br←Br) of 0 means that, during nursing, no gamma- and x-radiation emitted from activity within the maternal breast was absorbed within the maternal breast.

[C] The entry, "not applicable," means that the particular dose factor was not used in the dosimetric analysis of the particular radionuclide.

Table 3

Total Radiation Dose to the Nursing Child - Whole Body and, if Applicable, Thyroid - Assuming *No* Interruption of Breast-feeding and *Instantaneous* Uptake of Activity in Breast Milk

Radiopharmaceutical	A [a] (mCi)	$f_{breast\ milk}$	$f_{maternal\ rem}$ [b]	$(T_e)_{breast\ milk}$ (h)	$(T_e)_{maternal\ rem}$ (h)	Mean Whole-body Absorbed Dose to Newborn (rad)	Mean Thyroid Absorbed Dose to Newborn (rad)
^{11}C-Any radiopharmaceutical	25	0.05 [c]	0.95	0.333 [d]	0.333 [d]	0.251	not applicable
^{13}N-Any radiopharmaceutical	25	0.05 [c]	0.95	0.166 [d]	0.166 [d]	0.131	not applicable
^{15}O-Any radiopharmaceutical	50	0.05 [c]	0.95	0.0339 [d]	0.0339 [d]	0.131	not applicable
^{18}F-FDG [e]	10	0.04	0.96	1.83 [d]	1.83 [d]	0.385	not applicable
^{67}Ga-citrate [f]	5	0.10	0.90	78.2	78.2	62.3	not applicable
^{68}Ga-octreotate [g]	5	0.002	0.998	1.13 [d]	1.13 [d]	0.0218	not applicable
^{82}Rb-chloride	60	0.05 [c]	0.95	0.0212 [d]	0.0212 [d]	0.0396	not applicable
^{99m}Tc-Any radiopharmaceutical [h]	10	0.10	0.90	6.04 [d]	6.04 [d]	0.548	not applicable
	20	"	"	"	"	1.10	not applicable
	30	"	"	"	"	1.64	not applicable
^{111}In-octreotate [i]	5	3.04×10^{-5}	~1	10.8	48.0	5.41	not applicable
		1.39×10^{-5}		118			
^{111}In-white blood cells [f]	5	1.01×10^{-4}	~1	45.5	46.0	5.45	not applicable
^{123}I-ortho-iodohippurate (OIH) [f]	1	0.00852	0.991	3.50	0.617	0.333	not applicable
^{123}I-meta-iodobenzylguanidine (MIBG) [f]	11	0.00102	0.999	11.4	11.2	0.0720	not applicable
^{123}I-iodide [f]	0.4	0.0708	0.929	10.6	10.3	0.104	4.90
^{124}I-iodide [f]	2	0.0708	0.929	36.2	32.5	46.6	3,100
^{131}I-ortho-iodohippurate (OIH) [f]	0.27	0.00852	0.999	4.70	0.617	0.143	not applicable
^{131}I-meta-iodobenzylguanidine (MIBG) [f]	2	0.00102	0.999	59.0	54.5	1.66	not applicable
^{131}I-iodide [f]	2	0.0708	0.929	44.0	38.4	54.5	6,393
^{177}Lu-octreotate [j]	50	3.04×10^{-5}	~1	10.1	81.6	21.9	not applicable
		1.39×10^{-5}					
	211	3.04×10^{-5}	~1	10.1	81.6	5.20	not applicable
		1.39×10^{-5}					
^{201}Tl-thallous chloride [f]	4	2.75E-04	~1	27	57.6	0.353	not applicable

[a] The administered activity of each radiopharmaceutical was taken from Stabin MG, Breitz HB. Breast milk excretion of radiopharmaceuticals: mechanisms, findings and radiation dosimetry. J Nucl Med 2000; 41:863-873, the relevant Package Insert, or the reference cited. In some cases (e.g. 25 mCi for any ^{11}C- and any ^{13}N-labeled radiopharmaceutical), a "reasonably" conservative administered activity was assumed.

[b] The fraction of the administered activity in the maternal remainder of body, $f_{\text{maternal rem}}$, was calculated as 1- $f_{\text{breast milk}}$, where $f_{\text{breast milk}}$ is the maximum fraction of the administered activity in breast milk.

[c] For radiopharmaceuticals for which relevant data were not available, it was conservatively assumed that the maximum fraction of the administered activity in breast milk was 0.05.

[d] For radiopharmaceuticals for which relevant data were not available, it was conservatively assumed that the effective half-life of activity in breast milk and in the maternal remainder of body, $(T_e)_{\text{breast milk}}$ and $(T_e)_{\text{maternal rem}}$, respectively, equaled the physical half-life of the radioisotope.

[e] Kinetic parameters based on data in Hicks RJ, Binns D, and Stabin MG: Pattern of uptake and excretion of (18)F-FDG in the lactating breast. J Nucl Med. 42:1238-42, 2001.

[f] Kinetic parameters based on data in Stabin MG, Breitz HB. Breast milk excretion of radiopharmaceuticals: mechanisms, findings and radiation dosimetry. J Nucl Med 2000; 41:863-873.

[g] Kinetic parameters based on data in Forwood NJ, Kanthan GL, Bailey DL, Chan DL, and Schembri GP. ^{68}Ga-DOTATATE breast uptake and expression in breast milk. Clin Nucl Med 41: 654-655, 2016.

[h] The maximum fraction of all ^{99m}Tc-labeled radiopharmaceuticals in breast milk was conservatively set equal to 0.10, the maximum value in Stabin MG, Breitz HB. Breast milk excretion of radiopharmaceuticals: mechanisms, findings and radiation dosimetry. J Nucl Med 2000; 41:863-873.

[i] Kinetic parameters based on data in Castronovo FP, Jr., Stone H, and Ulanski J. Radioactivity in breast milk following ^{111}In-octreotide. Nucl Med Commun 21:695-9, 2000.

[j] The kinetic parameters for ^{177}Lu-octreotate were assumed to be the same as those for^{111}In-octreotide, as extracted from data in Castronovo FP, Jr., Stone H, and Ulanski J. Radioactivity in breast milk following ^{111}In-octreotide. Nucl Med Commun 21:695-9, 2000, except for the maternal remainder-of-body effective half-time, $(T_e)_{\text{maternal rem}}$, which was based on data in Said MA, Masud

MA, Zaini MZ, Salelh RA, Lee BN, and Zainon R. Lu-177 DOTATATE dosimetry for neuroendocrine tumor: Single center experience. J Phys Conf Ser 851: 012017.

Table 4

Duration of Discontinuation of Breast-Feeding to Achieve Specified Dose Limits to Newborn Tissue

Radiopharmaceutical	A [a] (mCi)	Dose-limiting Newborn Tissue	Duration of Discontinuation of Breast-feeding to Achieve the Following Dose to the Dose-limiting Newborn Tissue	
			0.1 rad	0.5 rad
^{11}C-Any radiopharmaceutical	25	Whole body	1 h	No discontinuation
^{13}N-Any radiopharmaceutical	25	Whole body	1 h	No discontinuation
^{15}O-water	50	Whole body	1 h	No discontinuation
^{18}F-FDG	10	Whole body	4 h	No discontinuation
^{67}Ga-citrate	5	Whole body	31 d	23 d
^{68}Ga-octreotate	5	Whole body	No discontinuation	No discontinuation
^{82}Rb-chloride	60	Whole body	No discontinuation	No discontinuation
^{99m}Tc-Any radiopharmaceutical	10	Whole body	16 h	4 h
	20	"	24 h	8 h
	30	"	32 h	16 h
^{111}In-octreotate	5	Whole body	5.7 d	7.5 d
^{111}In-white blood cells	5	Whole body	5.7 d	7.5 d
^{123}I-ortho-iodohippurate (OIH)	1	Whole body	4 h	No discontinuation
^{123}I-meta-iodobenzylguanidine (MIBG)	11	Whole body	No discontinuation	No discontinuation
^{123}I-iodide	0.4	Thyroid	2.7 d	1.5 d
^{124}I-iodide	2	Thyroid	28 d	21 d
^{131}I-ortho-iodohippurate (OIH)	0.27	Whole body	4 h	No discontinuation
^{131}I-meta-iodobenzylguanidine (MIBG)	2	Whole body	7.8 d	3.2 d
^{131}I-iodide	2	Thyroid	32 d	26 d
^{177}Lu-octreotate	50	Whole body	19 d	12 d
	211	"	27 d	19 d
^{201}Tl-thallous chloride	4	Whole body	4.3 d	No discontinuation

[a] The administered activity of each radiopharmaceutical was taken from Stabin MG, Breitz HB. Breast milk excretion of radiopharmaceuticals: mechanisms, findings and radiation dosimetry. J Nucl Med 2000; 41:863-873, the relevant Package Insert, or the reference cited. In some cases (e.g. 25 mCi for any ^{11}C- and any ^{13}N-labeled radiopharmaceutical and 50 mCi for ^{15}O-water), a "reasonably" conservative administered activity was assumed.

Table 5

Other Recommendations for Discontinuation of Breast-feeding in Nursing Mothers Undergoing Nuclear Medicine Procedures Based on a Dose Limit of 0.1 rad

Radiopharmaceutical	NRC NUREG 1556 Vol 9 Rev 3, Appendix U	ICRP Publication 106, Annex D	Stabin and Breitz, J Nucl Med 41: 863-873, 2000	MSKCC Recommendations, 2017
All ^{11}C-labeled radiopharmaceuticals	Not included	No interruption	Not included	Not included
All ^{13}N-labeled radiopharmaceuticals	Not included	No interruption	Not included	Not included
All ^{14}C-labeled radio-pharmaceuticals, including ^{14}C-urea	Not included	No interruption	Not included	Not included
All ^{15}O-labeled radiopharmaceuticals	Not included	No interruption	Not included	Not included
All ^{18}F-labeled radio-pharmaceuticals, including ^{18}F-FDG	Not included	No interruption	Not included	12 h
^{51}Cr-EDTA	No interruption	No interruption	No interruption	Not included
^{67}Ga-citrate	1 month for 4 mCi, 2 weeks for 1.3 mCi, 1 week for 0.2 mCi	> 21 d	Complete cessation for current child for 5 mCi	21 d
All ^{68}Ga-labeled radiopharmaceuticals	Not included	Not included	Not included	12 h
^{81m}Kr-gas	Not included	No interruption	Not included	Not included
^{82}Rb-chloride	Not included	Not included	Not included	Not included
^{89}Zr-antibodies	Not included	Not included	Not included	21 d
^{99m}Tc-DMSA	Not included	No interruption	Not included	24 h
^{99m}Tc-DTPA	No interruption	No interruption	No interruption	
^{99m}Tc-DTPA aerosol	No interruption	No interruption	No interruption	
^{99m}Tc-DISIDA	No interruption	No interruption	No interruption	
^{99m}Tc-ECD	Not included	No interruption	Not included	
^{99m}Tc-gluconate	Not included	No interruption	Not included	
^{99m}Tc-glucoheptonate	No interruption	No interruption	No interruption	
^{99m}Tc-HAM	Not included	No interruption	No interruption	
^{99m}Tc-MAG3	No interruption	No interruption	No interruption	
^{99m}Tc-MAA	13 h for 4 mCi	12 h	12 h for 4 mCi	
^{99m}Tc-MDP	No interruption	No interruption	No interruption	
^{99m}Tc-MIBI	No interruption	No interruption	No interruption	
^{99m}Tc-PYP	No interruption	No interruption	No interruption	
^{99m}Tc-RBCs - in vitro labeling	No interruption	No interruption	No interruption	
^{99m}Tc-RBCs - in vivo labeling	6 h for 20 mCi	12 h	12 h for 20 mCi	
^{99m}Tc-pertechnetate	24 h for 30 mCi, 12 h for 12 mCi	12 h	4 h for 5 mCi	

^{99m}Tc-sulfur colloid	6 h for 12 mCi	No interruption	No interruption	
^{99m}Tc-tetrofosmin	Not included	No interruption	Not included	
^{99m}Tc-WBCs	24 h for 30 mCi, 12 h for 12 mCi	12 h	No interruption	
^{111}In-antibodies	Not included	Not included	Not included	Not included
^{111}In-octreotide	Not included	No interruption	Not included	Not included
^{111}In-WBCs	7 d for 0.5 mCi	No interruption	No interruption	7 d
^{123}I-MIBG	24 h for 10 mCi, 12 h for 4 mCi	> 3 weeks	48 h for 10 mCi	7 d
^{123}I-NaI	No interruption	> 3 weeks	Complete cessation for current child	7 d
^{123}I-OIH	No interruption	12 h	No interruption	7 d
^{124}I-NaI	Not included	Not included	Not included	Complete cessation for current child
^{124}I-antibodies	Not included	Not included	Not included	Complete cessation for current child
^{125}I-OIH	No interruption	12 h	No interruption	Not included
^{131}I-OIH	No interruption	12 h	No interruption	Not included
^{131}I-NaI	Complete cessation for current child	>3 weeks to complete cessation for the current child	Complete cessation for current child	Complete cessation for current child
^{133}Xe-gas	Not included	No interruption	Not included	Not included
All ^{177}Lu-labeled radiopharmaceuticals	Not included	Not included	Not included	28 d for diagnostic activity, Complete cessation for the current child for therapeutic activity
^{201}Tl-chloride	14 d for 3 mCi	48 h	96 h for 3 mCi	14 d
All alpha particle-emitting radiopharmaceuticals, including ^{223}Ra-dichloride	Not included	Not included	Not included	Complete cessation for current child

References

[1] Fahey F, Zanzonico P, "Radiation Safety for Nursing Mothers Undergoing Nuclear Medicine Procedures", presentation, 49th Annual Conference of Radiation Control Program Directors, May 8-11, 2017.

[2] Kelly Mom Parenting Breastfeeding website

[3] US Nuclear Regulatory Commission Regulatory Guide 8.39: Release of Patients Administered Radioactive Materialsm, April 1997.

[4] Royal HD, Schwarz SW, Seigel BA: Case 17: Radiopharmaceutical Misadministration. In: Nuclear Radiology (Fifth Series) Test And Syllabus (Keyes JW, Brown ML, Miller TR, eds.), American College of Radiology, Reston, VA, 1998 pp 177-191.

[5] Chandra R Introductory Physics of Nuclear Medicine, 3rd edition. Philadelphia. 1990 p.34-37.

[6] Anderson PO Radiopharmaceuticals LactMed Update. Breastfeeding Medicine Vol 11(5):2016. Page 216-217.

[7] Ibid

[8] Ibid

[9] Anderson PO Radiopharmaceuticals LactMed Update. Breastfeeding Medicine Vol 11(5):2016. Page 216-217.

[10] Stabin MG, Breitz HB. Breast milk excretion of radiopharmaceuticals: mechanisms, findings and radiation dosimetry. J Nucl Med 2000; 41:863-873.

[11] Ibid

[12] Ibid

[13] Hedrick WR, Di Simone RN, and Keen RL: Radiation dosimetry from breast milk excretion of radioiodine and pertechnetate. J Nucl Med. 27:1569-71, 1986.

[14] Mountford PJ and Coakley AJ: Breast milk radioactivity following injection of 99Tcm-pertechnetate and 99Tcm-glucoheptonate. Nucl Med Commun. 8:839-45., 1987

[15] Mountford PJ and Coakley AJ: A review of the secretion of radioactivity in human breast milk: data, quantitative analysis and recommendations. Nucl Med Commun. 10:15-27, 1989.

[16] Mountford PJ, Coakley AJ, and Hall FM: Excretion of radioactivity in breast milk following injection of 99Tcm- DTPA. Nucl Med Commun. 6:341-5, 1985.

[17] Ogunleye OT: Assessment of radiation dose to infants from breast milk following the administration of 99mTc pertechnetate to nursing mothers. Health Phys. 45:149-51, 1983.

[18] Robinson PS, Barker P, Campbell A, et al.: Iodine-131 in breast milk following therapy for thyroid carcinoma [see comments]. J Nucl Med. 35:1797-801, 1994.

[19] Rubow S, Klopper J, Wasserman H, et al.: The excretion of radiopharmaceuticals in human breast milk: additional data and dosimetry [see comments]. Eur J Nucl Med. 21:144-53, 1994.

[20] Rumble WF, Aamodt RL, Jones AE, et al.: Accidental ingestion of Tc-99m in breast milk by a 10-week-old child. J Nucl Med. 19:913-5, 1978.

[21] Sharma SC, Osborne RP, Jose B, et al.: Dose estimation to the infant from breast milk following intraperitoneal administration of chromic phosphate 32P for the treatment of early ovarian cancer. Health Phys. 47:452-4, 1984.

[22] Siddiqui AR: Accidental ingestion of Tc-99m in breast milk by a 10-week-old child [letter]. J Nucl Med. 20:799, 1979.

[23] Simon SL, Luckyanov N, Bouville A, et al.: Transfer of 131I into human breast milk and transfer coefficients for radiological dose assessments. Health Phys. 82:796-806, 2002.

[24] Castronovo FP, Jr., Stone H, and Ulanski J: Radioactivity in breast milk following 111In-octreotide. Nucl Med Commun. 21:695-9, 2000.

[25] BEIR, Health Effects of Exposure to Low Levels of Ionizing Radiation (BEIR VII). Biological Effects of Ionizing Radiation (BEIR) Committee, National Research Council. 2006, Washington, DC: National Academies Press.

[26] Stabin MG, Breitz HB. Breast Milk Excretion of Radiopharmaceuticals: Mechanisms, Findings and Radiation Dosimetry. J Nucl Med 2000; 41:863-873.

[27] Stabin M, Watson E, Cristy M, et al., Mathematical Models and Specific Absorbed Fractions of Photon Energy in the Nonpregnant Adult Female and at the End of Each Trimester of Pregnancy. 1995, Oak Ridge National Laboratoies: Oak Ridge, TN

[28] Hicks RJ, Binns D, and Stabin MG: Pattern of uptake and excretion of (18)F-FDG in the lactating breast. J Nucl Med. 42:1238-42, 2001.

[29] Stabin MG, Sparks RB, and Crowe E: OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med. 46:1023-7, 2005.

[30] Cristy M and Eckerman K, Specific absorbed fractions of energy at various ages from internal photon sources (I-VII). Oak Ridge National Laboratory Report ORNL/TM-8381/V1-7. 1987, Springfield, VA: National Technical Information Service, Dept of Commerce.

[31] Stabin MG, Breitz HB. Breast Milk Excretion of Radiopharmaceuticals: Mechanisms, Findings and Radiation Dosimetry. J Nucl Med 2000; 41:863-873.

[32] Ibid

[33] Luster M, Clarke SE, Dietlein M, et al.: Guidelines for radioiodine therapy of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging. 35:1941-59, 2008.

[34] Fact Sheet: Guidelines for Patients Receiving Radioiodine I-131 Treatment. Available from: http://snmmi.files.cms-plus.com/FileDownloads/Patients/FactSheets/Radio_.pdf.

[35] Smith DS and Stabin MG. Exposure rate constants and lead shielding values for over 1,100 radionuclides. Health Phys 102: 271-291, 2012.

[36] The distance from the mother's breast to the nursing child, $r_{\text{breast-to-child}}$, corresponds to the assumed approximate distance from the mid-line of the mother's breast (i.e., for the Reference Adult Female anatomic phantom) to the mid-line of the child (i.e., the Reference Newborn anatomic model). This is the sum of the one-half of the "a" parameter value, 1/2 • 5 cm =2.5 cm, tabulated for the Reference Adult Female and the "B_T" parameter value, 2.5 cm, for the Reference Newborn referenced in Cristy M and Eckerman K, Specific absorbed fractions of energy at various ages from internal photon sources (I-VII). Oak Ridge National Laboratory Report ORNL/TM-8381/V1-7. 1987, Springfield, VA: National Technical Information Service, Dept of Commerce.

[37] The distance from the mother's torso to the nursing child, $r_{\text{maternal rem-to-child}}$, corresponds to the assumed approximate distance from the mid-line of the mother (i.e., for the Reference Adult Female anatomic phantom) to the mid-line of the child (i.e., the Reference Newborn anatomic model). This is the sum of the "B_T" parameter values, 5 and 10 cm respectively to include conversion factor referenced in Cristy M and Eckerman K, Specific absorbed fractions of energy at various ages from internal photon sources (I-VII). Oak Ridge National Laboratory Report ORNL/TM-8381/V1-7. 1987, Springfield, VA: National Technical Information Service, Dept of Commerce.

[38] In order to model the maternal breast activity as a line source, rather than a point source, a conversion factor is required to appropriately adjust the inverse-square dependence on distance of the point-source dose rate. This conversion factor depends on the length of the line source, which is 5 cm for the breast line source, and the distance from the line source, which is $r_{\text{breast-to-child}} = 7.5$ cm for the mid-line of the nursing child.

The length of the breast line source is equated with parameter "c" tabulated for the Reference Adult Female anatomic model referenced in Cristy M and Eckerman K, Specific absorbed fractions of energy at various ages from internal photon sources (I-VII). Oak Ridge National Laboratory Report ORNL/TM-8381/V1-7. 1987, Springfield, VA: National Technical Information Service, Dept of Commerce.

The conversion factor is taken from Siegel JA, Marcus CS, and Sparks RB: Calculating the absorbed dose from radioactive patients: the line-source versus point-source model. J Nucl Med. 43:1241-4, 2002, Table 1.

[39] For the point source-to-line source conversion factor for the maternal torso-to-child exposure, the length of the line source is 63 cm for the maternal torso and the distance from the line source is $r_{mother\text{-}to\text{-}child} = 15$ cm. The length of the maternal torso line source is equated with parameter "C_T" tabulated for the Reference Adult Female anatomic model referenced in Cristy M and Eckerman K, Specific absorbed fractions of energy at various ages from internal photon sources (I-VII). Oak Ridge National Laboratory Report ORNL/TM-8381/V1-7. 1987, Springfield, VA: National Technical Information Service, Dept of Commerce.

[40] An occupancy factor for nursing, $E_{nursing}$, of 0.33 conservatively assumes that the child will actually be nursing for 8 hours out of each day (24 hours).

[41] Siegel JA, Marcus CS, and Sparks RB: Calculating the absorbed dose from radioactive patients: the line-source versus point-source model. J Nucl Med. 43:1241-4, 2002.

[42] Stabin MG, Breitz HB. Breast Milk Excretion of Radiopharmaceuticals: Mechanisms, Findings and Radiation Dosimetry. J Nucl Med 2000; 41:863-873.

[43] Ibid

[44] Zanzonico, PB. Age-dependent thyroid absorbed doses for radiobiologically significant radioisotopes of iodine. Health Phys 78: 60-67, 2000.

[45] Zanzonico, PB. Age-dependent thyroid absorbed doses for radiobiologically significant radioisotopes of iodine. Health Phys 78: 60-67, 2000.

[46] Polgar C and Major T: Current status and perspectives of brachytherapy for breast cancer. Int J Clin Oncol. 14:7-24, 2009.

[47] Smith BD, Arthur DW, Buchholz TA, et al.: Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int J Radiat Oncol Biol Phys. 74:987-1001, 2009.

[48] Smith GL, Xu Y, Buchholz TA, et al.: Brachytherapy for accelerated partial-breast irradiation: a rapidly emerging technology in breast cancer care. J Clin Oncol. 29:157-65, 2011.

[49] Thomson W, Mills A, Smith N, et al.: Day and night radiation doses to patients' relatives: Implications of ICRP 60 (Abstract). Nucl Med Commun. 14:275, 1993

[50] Edeline J, Gilabert M, Garin E, et al.: Yttrium-90 microsphere radioembolization for hepatocellular carcinoma. Liver Cancer. 4:16-25, 2015.

[51] Zanzonico PB, Binkert BL, and Goldsmith SJ: Bremsstrahlung radiation exposure from pure beta-ray emitters. J Nucl Med. 40:1024-8, 1999.

[52] Jakub JW, Gray RJ, Degnim AC, et al.: Current status of radioactive seed for localization of non palpable breast lesions. Am J Surg. 199:522-8, 2010.

[53] Gray RJ, Pockaj BA, Karstaedt PJ, et al.: Radioactive seed localization of nonpalpable breast lesions is better than wire localization. Am J Surg. 188:377-80, 2004.

[54] NRC, Consolidated Guidance About Materials Licenses Program-Specific Guidance About Medical Use Licenses, Draft Report for Comment, NUREG-1556, Volume 9, Rev. 3, N.R. Commission, Editor. 2016: Rockville, MD.

[55] ICRP: Annex D. Recommendations on Breat-Feeding Interruptions. Radiation Dose to Patients from Radiopharmaceuticals. A Third Amendment to ICRP Publication 53. Annals of the ICRP. 38:163-165, 2008.

[56] Center MSKC, Policy and Procedure L1208 - Lactating Mothers Receiving Radiopharmaceuticals. 2017: New York, NY.

[57] Johns H and Cunningham J, The Physics of Radiology. 1974, Springfield, IL: Charles C Thomas. pp 276-277.

[58] Except for ^{18}F-FDG, the breast absorbed doses are taken from Stabin MG and Breitz HB: Breast milk excretion of radiopharmaceuticals: mechanisms, findings, and radiation dosimetry. J Nucl Med. 41:863-73, 2000. The ^{18}F-FDG breast absorbed doses were calculated based on the referenced data from Hicks RJ, Binns D, and Stabin MG: Pattern of uptake and excretion of ^{18}F-FDG in the lactating breast. J Nucl Med. 42:1238-42, 2001.

[59] For radiopharmaceuticals which only a single breast absorbed dose is available in the literature, the absorbed dose is listed in the "Highest Estimate" column.

[60] The physical half-lives and gamma- and x-ray energies are taken from Eckerman K and Endo A. MIRD Radionuclide Data and Decay Schemes, 2nd ed. Society of Nuclear Medicine, Reston, VA, 2007. The specific gamma-ray constants are taken from Smith DS and Stabin MG. Exposure rate constants and lead shielding values for over 1,100 radionuclides. Health Phys 102: 271-291, 2012. The absorbed fractions are taken from Cristy M and Eckerman KF. Specific Absorbed Fractions of Energy at Various Ages from Internal Sources. V. Fifteen-Year-

Old Male and Adult female, ORNL/TM-8381/V5, Oak Ridge National Laboratory, Oak Ridge, TN, 1987. The dose factors (also known as S values) are taken from Stabin MG, Sparks RB, and Crowe E: OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med. 46:1023-7, 2005.