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

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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 dosimetric analyses in this section assume that there is no interruption of breast-feeding following administration of the radiopharmaceutical to the mother.

(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 maternal milk containing radioactivity. 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

$D_{nursing\ child \leftarrow maternal\ rem}|_{ext}$ = 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, $D_{nursing\ child \leftarrow maternal\ breast}|_{ext}$, and in theremainder of the mother's body, $D_{nursing\ child \leftarrow maternal\ rem}|_{ext}$, can be calculated by Equations (2) and (3), respectively:

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

and

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

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

$\tau_{maternal\ rem}$ = 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),

$r_{breast\text{-}to\text{-}child}$ = 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,

$r_{maternal\ rem\text{-}to\text{-}child}$ = 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,

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

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

$\phi(breast\text{-}to\text{-}breast)$ = the breast-to-breast photon absorbed fraction,

$\phi(maternal\ WB\text{-}to\text{-}maternal\ WB)$

= the maternal whole body (WB)-to-maternal whole body (WB) photon absorbed fraction, and $E_{nursing}$ = the occupancy factor for nursing.

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 cumulative 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,

$F_{maternal\ rem}$ = 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 $(T_e)_i|_{breast\ milk}$ = the effective 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[35]. 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, generallyless 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[36]. Higher cumulative excretions been reported only with ^{67}Ga-citrate and ^{131}I-NaI up to ~10 and ~25%, respectively[37]. Based on the cumulative fraction of the administered activity in breast milk and the half-time(s) of clearance from breast milk (Table 3), 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, $D_{\text{nursing child}}\big|_{\text{int}}$, can then be derived using equation (6):

$$D_{\text{nursing child}}\big|_{\text{int}} = \tau_{\text{breast milk}} \bullet DF(WB \leftarrow WB)_{\text{newborn}} \qquad (6)$$

where

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

Implicit in the dose estimates shown in Table 3 is that breast-feeding was *not* interrupted following administration of the radiopharmaceutical to the nursing mother.

(c) Total Radiation Dose to the Nursing Child

The total radiation doses to a nursing child for various radiopharmaceuticals administered to the mother, calculated by summing the respective external and internal radiation doses, are presented in Table 4; these represent the mean whole-body absorbed doses to the child. The calculated absorbed doses to the nursing child if breast-feeding were *not* interrupted uniformly exceed 0.1 rad (= 100 mrad), and thus the 100-mrem (1-mSv) maximum recommended dose limit for a nursing child.

Despite the conservative assumptions implicit in estimating the doses for ^{18}F-FDG and ^{99m}Tc-labeled radiopharmaceuticals, these doses only slightly exceed the 100-mrem dose limit. ^{67}Ga-citrate and ^{131}I-NaI doses, however, exceed the 100-mrem dose limit by more than an order of magnitude and with ^{131}I-NaI therapy by several orders of magnitude. Therefore, with the exception of ^{131}I-NaI and several other radiopharmaceuticals (See "Precautions for Nursing Mothers: Recommendations and Rationale" and Table 5 below), a brief temporary discontinuation of breast-feeding following maternal radiopharmaceutical administration is sufficient to maintain the nursing child's radiation dose below the 100-mrem (1-mSv) dose limit.

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 will be 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 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 2, 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, 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[38 39 40]. 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[41 42]. 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[43]. 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[44 45]. RSL is an alternative to the traditional needlewire 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[46], the International Commission on Radiological Protection (ICRP)[47], and others[48] are based on a maximum dose (i.e., dose equivalent) to the nursing child of 100 mrem (0.1 rem). As summarized in Table 5, the extant recommended precautions for nursing mothers are somewhat variable in terms of both the radiopharmaceutical and the time interval for breast feeding interruption following radiopharmaceutical administration to the nursing mother. The cited NRC and ICRP recommendations are the most current and up-to-date.

In formulating the current recommendations – listed in the last column in Table 5 – our Sub-Committee generally selected the most conservative existing recommendation, which was usually the longest interruption period for each radiopharmaceutical. 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 interruption period of 24-hours is recommended. Although this time interval may be longer than absolutely necessary for some ^{99m}Tc-labeled radiopharmaceuticals, it is compliant with the 100-mrem dose limit and simplifies the guidance, thereby avoiding confusion and reducing the likelihood of error.

2. For ^{18}F-FDG, all other ^{18}F-labeled and all gallium-68 (^{68}Ga)-labeled radiopharmaceuticals, a 12-hour interruption period is recommended. This conservative recommendation is cautious and simplifies safety instructions for patients and medical professionals. A 12-hour interruption period is recommended for ^{68}Ga for the following reasons: (a) a physical half-life comparable to that of ^{18}F, (b) the propensity of free

radiogallium to accumulate in breast milk and (c) the lack of relevant data on ^{68}Ga-labeled agents in nursing mothers.

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 after the procedure is completed.

4. For iodine-123 in the form of NaI (^{123}I-NaI), an interruption period of 7 days is recommended. This is in marked contrast to the past, where complete cessation of breast-feeding for the current child was recommended. This older, more stringent ^{123}I-NaI recommendation was largely 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[49]. Such contamination of ^{123}I with ^{125}I no longer occurs. Therefore, the restrictions on breast-feeding following ^{123}I-NaI administration to the nursing mother may be justifiably relaxed to an interruption period of 7 days.

5. 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 an interruption period of 7 days and for thallium-201 (^{201}Tl-chloride) an interruption period of 14 days are recommended. These recommendations mirror that of the NRC in the Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses, NUREG-1556, Vol 9, Rev 1, Appendix U, 2005.

6. 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.

   For lutecium-177 (^{177}Lu), based on the foregoing ^{89}Zr rationale and a longer physical half-life (6.65 days), an interruption period of 35-days (i.e., 5 weeks) is recommended for ^{177}Lu-labeled radiopharmaceuticals used *diagnostically*. For ^{177}Lu-labeled radiopharmaceuticals used *therapeutically*, much higher activities are administered, and thus, permanent cessation of breast-feeding for the current child is recommended.

7. 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 Cessation**
^{11}C, ^{13}N, ^{15}O, ^{82}Rb	None
^{18}F-labeled	12-hours
^{68}Ga-labeled	12-hours
^{99m}Tc-labeled	24-hours
^{123}I-NaI	7 days
^{111}In-leukocytes	7 days
^{201}Tl-chloride	14 days
^{67}Ga and ^{89}Zr	28 days
^{177}Lu, diagnostic	35 days
^{131}I-NaI	Stop breast feeding
^{177}Lu, 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 signage used to alert pregnant and potentially pregnant patients to possible hazards of nuclear medicine and radiological procedures, the following or equivalent signage 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

	Administered Activity		Breast Absorbed Dose[50 51]			
			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	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

Table 2

Estimation of the External Radiation Dose from the Mother to the Nursing Child Assuming No Interruption of Breast-feeding: Model Parameters

	^{18}F-FDG	**^{67}Ga-citrate**	**^{99m}Tc "Worst case"**	**^{131}I-NaI**
Photon energy (keV)	511	93, 185, 300	140	364
Physical half-life (h)	1.2	78.2	6.04	193
Specific Gamma-ray Constant, G (R-cm^2/mCi-h)[52]	0.0057	0.00080	0.00060	0.0022
Administered Activity (mCi), A - Assumed	10	5	30	5 (imaging), 150 (therapy)
Cumulative fraction of activity in breast milk, $f_{breast\ milk}$	0.040[53]	0.10[54]	0.05[55]	0.25[56]
Fraction of activity in remainder of body, $f_{maternal\ rem}$[57]	0.96	0.90	0.95	0.75
Maternal whole body-to-whole body photon absorbed fraction, f(maternal WB¬maternal WB)[58]	0.34	0.31	0.31	0.31
Maternal breast-to-breast photon absorbed fraction, f(Br¬Br)[59]	0	0	0	0
Effective half-time of activity in breast, $(T_e)_{breast\ milk}$ (h)[60]	1.2	78.2	6.02	10.4 (99%)
				81.8 (1%)
Effective half-life of activity in maternal remainder of body, $(T_e)_{maternal\ rem}$ (h)[61]	1.2	78.2	6.02	38.4
Distance from mother's breast to nursing child, $r_{breast\text{-}to\text{-}child}$ (cm)[62]			7.5	
Point source-to-line source conversion factor for maternal breast-to-child exposure, $CF_{point\text{-}to\text{-}line\|breast}$[63]			0.32	
Distance from mother's torso to nursing child, $r_{maternal\ rem\text{-}to\text{-}child}$ (cm)[64]			15	
Point source-to-line source conversion factor for maternal torso-to-child exposure, $CF_{point\text{-}to\text{-}line\|maternal\ rem}$[65]			0.54	
Occupancy factor for nursing, $E_{nursing}$[66]			0.33	

Table 3

Internal Radiation Dose to the Nursing Child from Ingestion of Radioactive Milk Assuming No Interruption of Breast-feeding: Model and Kinetic Parameters and Radiation Dose Estimates

Radiopharmaceutical	Assumed Administered Activity (mCi)	Cumulative Fraction Excreted in Breast Milk, ($f_{breast\ milk}$)	Effective Half-Time in Breast Milk, $(T_e)_i$ [1] hours	Residence Time in Breast Milk $\tau_{breast\ milk}$[67] (µCi-h/µCi)	Reference Newborn Whole Body-to-Whole Body Dose Factor $(DF(WB \leftarrow WB)_{newborn}$[68] rad/µCi-h)	Newborn Whole-Body Absorbed Doses, $D_{nursing\ child}\|_{int}$	
						rad/mCi	rad/Administered Activity
^{18}F-FDG	10	0.04[69]	1.2[70]	0.048	2.44E-04	0.012	0.12
^{67}Ga-citrate	5	0.10[71]	78.2[72]	7.8	3.68E-05	0.29	1.4
^{99m}Tc, "Worst case"	30	0.05[73]	6.02[74]	0.30	2.16E-05	0.0065	0.19
^{131}I-NaI	5 (imaging), 150 (therapy)	0.25[75]	10.4 (99%)[76] 81.8 (1%)	2.78	1.53E-04	0.43	2.2, 65

Table 4

Total Radiation Dose to the Nursing Child Assuming No Interruption of Breast-feeding

Radiopharmaceutical	Assumed Administered Activity mCi	Whole-Body Absorbed Dose to Nursing Child rad		
		External	Internal	Total
^{18}F-FDG	10	0.027	0.12	0.15
^{67}Ga-citrate	5	0.17	1.4	1.6
^{99m}Tc, "Worst case"	30	0.044	0.19	0.23
^{131}I-NaI	5 (imaging)	0.2	2.2	2.4
	150 (therapy)	5.3	65	70

Table 5

Recommendations for Cessation of Breast-feeding in Nursing Mothers Undergoing Nuclear Medicine Procedures

<table>
<tr><th>Radiopharmaceutical</th><th>NRC NUREG 1556 Vol 9 Rev 3, Appendix U</th><th>ICRP Publication 106, Annex D</th><th>Hazel and Breitz, J Nucl Med 41: 863-873, 2000</th><th>MSKCC Recommendations, 2017</th><th>Current ACMUI Sub-Committee Recommendations, 2017</th></tr>
<tr><td>All ^{11}C-labeled radiopharmaceuticals</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>All ^{13}N-labeled radiopharmaceuticals</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>All ^{14}C-labeled radio-pharmaceuticals, including ^{14}C-urea</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>All ^{15}O-labeled radiopharmaceuticals</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>All ^{18}F-labeled radio-pharmaceuticals, including ^{18}F-FDG</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>12 h</td><td>No interruption</td></tr>
<tr><td>^{51}Cr-EDTA</td><td>No interruption</td><td>No interruption</td><td>No interruption</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>^{67}Ga-citrate</td><td>1 month for 4 mCi, 2 weeks for 1.3 mCi, 1 week for 0.2 mCi</td><td>> 21 d</td><td>Complete cessation for current child for 5 mCi</td><td>21 d</td><td>28 d</td></tr>
<tr><td>All ^{68}Ga-labeled radiopharmaceuticals</td><td>Not included</td><td>Not included</td><td>Not included</td><td>12 h</td><td>12 h</td></tr>
<tr><td>^{81m}Kr-gas</td><td>Not included</td><td>No interruption</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>^{82}Rb-chloride</td><td>Not included</td><td>Not included</td><td>Not included</td><td>Not included</td><td>No interruption</td></tr>
<tr><td>^{89}Zr-antibodies</td><td>Not included</td><td>Not included</td><td>Not included</td><td>21 d</td><td>21 d</td></tr>
<tr><td>^{99m}Tc-DMSA</td><td>Not included</td><td>No interruption</td><td>Not included</td><td rowspan="19">24 h</td><td rowspan="19">24 h</td></tr>
<tr><td>^{99m}Tc-DTPA</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-DTPA aerosol</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-DISIDA</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-ECD</td><td>Not included</td><td>No interruption</td><td>Not included</td></tr>
<tr><td>^{99m}Tc-gluconate</td><td>Not included</td><td>No interruption</td><td>Not included</td></tr>
<tr><td>^{99m}Tc-glucoheptonate</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-HAM</td><td>Not included</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-MAG3</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-MAA</td><td>13 h for 4 mCi</td><td>12 h</td><td>12 h for 4 mCi</td></tr>
<tr><td>^{99m}Tc-MDP</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-MIBI</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-PYP</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-RBCs - in vitro labeling</td><td>No interruption</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-RBCs - in vivo labeling</td><td>6 h for 20 mCi</td><td>12 h</td><td>12 h for 20 mCi</td></tr>
<tr><td>^{99m}Tc-pertechnetate</td><td>24 h for 30 mCi, 12 h for 12 mCi</td><td>12 h</td><td>4 h for 5 mCi</td></tr>
<tr><td>^{99m}Tc-sulfur colloid</td><td>6 h for 12 mCi</td><td>No interruption</td><td>No interruption</td></tr>
<tr><td>^{99m}Tc-tetrofosmin</td><td>Not included</td><td>No interruption</td><td>Not included</td></tr>
<tr><td>^{99m}Tc-WBCs</td><td>24 h for 30 mCi, 12 h for 12 mCi</td><td>12 h</td><td>No interruption</td></tr>
</table>

^{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	7 d
^{111}In-octreotide	Not included	No interruption	Not included	Not included	24 h
^{111}In-WBCs	7 d for 0.5 mCi	No interruption	No interruption	7 d	7 d
^{123}I-MIBG	24 h for 10 mCi, 12 h for 4 mCi	> 3 weeks	48 h for 10 mCi	7 d	48 h
^{123}I-NaI	No interruption	> 3 weeks	Complete cessation for current child	7 d	48 h
^{123}I-OIH	No interruption	12 h	No interruption	7 d	No interruption
^{124}I-NaI	Not included	Not included	Not included	Complete cessation for current child	Complete cessation for current child
^{124}I-antibodies	Not included	Not included	Not included	Complete cessation for current child	Complete cessation for current child
^{125}I-OIH	No interruption	12 h	No interruption	Not included	No interruption
^{131}I-OIH	No interruption	12 h	No interruption	Not included	Complete cessation for current child
^{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	Complete cessation for current child
^{133}Xe-gas	Not included	No interruption	Not included	Not included	No interruption
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	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	14 d
All alpha particle-emitting radiopharmaceuticals, including ^{223}Ra-dichloride	Not included	Not included	Not included	Complete cessation for current child	Complete cessation for current child

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

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[59] It is conservatively assumed that the maternal breast does not attenuate any of the photon radiation emitted from the breast.

[60] For short-lived ^{18}F and ^{99m}Tc, the effective half-time in breast milk, (Te)breast milk, is conservatively equated with the respective physical half-life. For ^{131}I, the bi-exponential time-activity function with the effective half-times listed is referenced in 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.

[61] For short-lived ^{18}F and ^{99m}Tc, the effective half-time in maternal remainder of body, $(Te)_{maternal\ rem}$, is conservatively equated with the respective physical half-life. For ^{131}I, the whole-body biological half-time in a post-thyroidectomy thyroid cancer patient was assumed to be 2 days (or 48 hours).

[62] The distance from the mother's breast to the nursing child, $r_{breast\text{-}to\text{-}child}$, 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, $1/2 \cdot 5$ 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.

[63] 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 $r_{breast\text{-}to\text{-}child}$ = 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.

[64] The distance from the mother's torso to the nursing child, $r_{maternal\ rem\text{-}to\text{-}child}$, 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 res[ectively 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.

[65] See Note 63. 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.

[66] An occupancy factor for nursing, $E_{nursing}$, of 0.25 conservatively assumes that the child will actually be nursing for 6 hours out of each day (24 hours).

[67] $$\tau_{breast\ milk} = 1.44 \bullet F_{breast\ milk} \bullet \sum_{i=1}^{n} f_i|_{breast\ milk} \bullet (T_e)_i|_{breast\ milk}$$

[68] 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. Whole body-to-whole body dose factors, DF(WB¬WB)newborn, were taken from the OLINDA computer program in 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.

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