

# Application of acoustic radiation force impulse imaging (ARFI) in quantitative evaluation of neonatal brain development

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## Summary

**Objective:** This study aims to quantitatively evaluate the effect of acoustic radiation force impulse imaging (ARFI) in neonatal brain development. **Materials and Methods:** The authors observed 41 neonatal brain different tissues by using traditional two-dimensional gray scale ultrasound and color Doppler flow imaging and frequency spectrum ultrasound. After that they used ARFI to quantitative evaluate white and gray matter of neonatal different tissues in brain with different gestational ages. They also used new technical index: virtual touch tissue quantification (VTQ) to evaluate elastic changes of brain tissues. **Results:** Different tissues in brain had different elastic numerical values. Neonatal with different gestational ages had different elastic numerical values. The more gestational ages were, the more the elastic numerical values. Elastic numerical values between preterm and full-term infants were different. Elastic numerical values of full-term infants were higher than preterm infants. **Conclusion:** ARFI provides a new quantitative index to evaluate neonatal brain development. It increases objectivity and reliability of clinical analysis. Ultrasound was a noninvasive examination method, safe, simple, and convenient, and it has more usefulness of ARFI in quantitative evaluation of neonatal brain development.

**Key words:** Neonatal; Brain development; Acoustic radiation force impulse imaging.

## Introduction

Neonatal brain tissue and the function is in the process of development, and as a result of the existence of a variety of diseases, brain development can be blocked or brain damage, cause the functional and structural abnormalities, clinical manifestation of cerebral palsy, epilepsy and other neurological diseases [1-3]. Neonatal head ultrasound in neonatal cerebral disease diagnosis is of great significance, through analyzing the characteristics of the cerebral ultrasound, observation of brain volume size, the width of the gyri and craniocerebral overall the echo intensity, can evaluate neonatal brain development mature conditions, and change with gestational age can present different characteristics [4-7]. However, how to quantify the change to guide the evaluation of the degree of brain development is still a clinical problem remaining to be solved [8-10]. Acoustic radiation force impulse imaging (ARFI) is a good method for us in evaluating the maturity of infants' brain. Now ARFI has been widely used in liver, kidney, thyroid, breast, pancreas and so on [11-16]. However, ARFI has been little used in brain. This article analyzed quantitatively neonatal cerebral white and gray matter with different gestational ages by Virtual touch tissue quantification (VTQ) of ARFI, and discussed the value of VTQ to evaluate neonatal brain development.

## Materials and Methods

### Patients

Forty-one consecutive newborns were selected from the department of gynecology and obstetrics of First Hospital Affiliated to Shanghai Jiaotong University from March 2012 to October 2012; male 22 cases, female 19 cases, gestational ages < 37 weeks 16 cases, ≥ 37 weeks 25 cases. All neonates were appropriate for gestational ages (AGA). The exclusion criterion were jaundice of the newborn, aspiration pneumonia, neonatal brain injury and pregnancy complicated with diabetes mellitus, pregnancy induced hypertension, anemia and heart and lung diseases, *et al.* This study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Shanghai First People's Hospital, School of Medicine, Shanghai Jiaotong University. Written informed consent was also obtained from all participants before ARFI examination.

### Acquisition of the ARFI

Real-time ARFI was performed by using diagnostic ultrasound system equipped with 4C1 (3.5 MHz) probe. All the examinations were performed in succession by two independent sonographers. Both of them had more than ten years' experiences in ultrasonic scanning. They were blinded to the colposcopic findings and physical exam results when performing.

### Conventional ultrasound

Neonates that were born in one to three days were placed in a supine position in a quiet state. All participants were examined by brain US using the anterior fontanelle as the acoustic window. Conventional sonography was used to observe skull continuity, midline brain was centered, echo of brain parenchyma, lateral



Figure 1. — The value of VTQ of different parts of brain tissues in full-term infants. A) The value of VTQ of parietal white matter in full-term infants was 1.26 m/s; B) the value of VTQ of thalamic and basal ganglia in full-term infants was 1.46 m/s; C) the value of VTQ of cerebellum in full-term infants was 1.65 m/s.

Table 1. — Comparison of VTQ between preterm and full term infants.

Position	VTQ (m/s)		<i>p</i>
	<37 w	≥37 w	
Parietal white matter	1.12 ± 0.43	1.34 ± 0.33	< 0.05
Thalamic	1.21 ± 0.51	1.53 ± 0.35	< 0.05
Cerebellum	1.33 ± 0.41	1.62 ± 0.31	< 0.05
Cerebral falx	1.95 ± 0.52	2.23 ± 0.48	< 0.05

ventricle, cerebral transverse diameter, lateral ventricle width, and superior frontal gyrus width were measured. Color Doppler was used to access the blood supply of the brains. Including middle cerebral artery, anterior cerebral artery, posterior cerebral artery and vertebral basilar artery.

#### ARFI

Switching to the ARFI elastic model, VTQ was used to measure the elasticity of neonatal cerebral white and gray matter, which included parietal white matter, thalamic and basal ganglia, cerebellum, a hippocampus, medulla oblongata, and cerebral falx.

#### Virtual touch tissue quantification

In the VTQ model, ROI (5×10 mm) was placed inside the brain and the depth of the regions of interest (ROI) was less than 80 mm. All the structures of newborns brain were observed. For more accurate and objectively derived elastic parameters, operators were asked to handle with care and probe on the cranial surface. It was continuously measured three times randomly, and the average value was calculated as the VTQ value (meter per second). Care was taken to avoid vascular structures when measured.

#### Statistical analysis

All statistical analysis used SPSS version 17.0 software. All measured data are presented as the mean ± standard deviation. Groups of premature infants and full-term infants were compared using the Student U test and Analysis of variance. A *p* < 0.05 was considered statistically significant.

## Results

#### Echo intensity quantitative analysis

The authors used VTQ to quantitative analysis echo intensity in different parts of brain tissues. It showed that the value of VTQ of parietal white matter was  $1.34 \pm 0.33$  m/s,



Figure 2. — The value of VTQ of cerebellum in preterm infants was 0.84 m/s.

thalamic and basal ganglia were  $1.53 \pm 0.35$  m/s, cerebellum was  $1.62 \pm 0.31$  m/s, and cerebral falx was  $2.23 \pm 0.48$  m/s (Figure 1A-C).

#### Brain echo intensity

The authors measured the value of VTQ of echo intensity in different parts of brain tissues in different gestational ages of 41 infants; it showed that the value of VTQ of parietal white matter, thalamic and basal ganglia, cerebellum and cerebral falx gradually increased with increased gestational ages. The value of VTQ of preterm infants were obviously lower than full term infants (*p* < 0.05) (Table 1, Figure 2).

## Discussion

ARFI is a new elastic imaging technology, it uses acoustic radiation force to fire pulse, and it can cause instantaneous (<1 s) and tiny micron displacement in ROI of the body. At the same time, it produces shear wave at transverse vibration. The computer can test and calculate the speed of shear wave, which is called shear wave velocity and shear wave velocity is on behalf of the elasticity of tissue. The higher the

shear wave velocity is, the larger the coefficient of elasticity is. This is VTQ of ARFI, It does not rely on the pressure of the probe, so it has more objectively [17-21]. This technology can be utilized to quantitatively evaluate the echo intensity of neonatal brain.

From the present study, brain tissue of different parts of echo intensity quantitative analysis in full-term infants showed that the value of VTQ of parietal white matter was  $1.34 \pm 0.33$  m/s, thalamic and basal ganglia was  $1.53 \pm 0.35$  m/s, cerebellum was  $1.62 \pm 0.31$  m/s, and cerebral falx was  $2.23 \pm 0.48$  m/s. The proportion of increase was accordance with brain development. It can be more intuitive to understanding the situation of echo intensity in different brain tissues.

The brain development originates in ectoderm. Myelination of brain takes place at about 20 weeks of gestational ages. From the bottom to top, from central to peripheral, from dorsal to ventral, from sensory fibers into motor fibers. That is to say, the development of myelination of brain is from brain stem to thalamic and basal ganglia to each lobe of brain. It suggests that development of thalamus and cerebral falx were more early and mature [22, 23].

The present results show that different brain echo intensity occur at different gestational ages. The value of VTQ in preterm infants were obviously lower than that of in full term infants. Brain development in preterm infants are more immature than full term infants [24, 25].

Neonatal head ultrasound is with the aid of before and after anterior fontanelle and lateral anterior fontanelle as the acoustic window, for cerebral coronal and sagittal scans. Its advantages include bed check, no radiation damage and low cost, do not need to be calm, can be repeated many times, and is the first choice for the premature infant brain injury. Its disadvantages are the need of the operator to have experience and has certain limitations of craniocerebral peripheral lesions. Therefore, it remains to be combined with other imaging examination methods such as MRI [26, 27].

In conclusion, the value of VTQ is a very useful quantitative index in evaluation of the neonate brain development. ARFI is a safe, noninvasive, simple, and convenient technology; it can play a greater role not only in evaluation of the neonate brain development, but in diagnosing diseases in neonate brain, including preterm, and full term infants, and will be the topic of the present authors' future study. While ARFI is still in the preliminary clinical application stage, more cases must be observed to accumulate experience.

## Acknowledgements

The authors want to thank the paediatricians who provided clinical data for this study. They also thank Xia Jin, Fang Min, Gao LinLin, *et al*, from the Newborn Department of Pediatrics of the present hospital, for their helpful contributions.

## References

- [1] Salmasso N., Tomasi S., Vaccarino FM.: "Neurogenesis and maturation in neonatal brain injury". *Clin. Perinatol.*, 2014, 41, 229.
- [2] Kwon S.H., Vasung L., Ment L.R., Huppi P.S.: "The role of neuroimaging in predicting neurodevelopmental outcomes of preterm neonates". *Clin. Perinatol.*, 2014, 41, 257.
- [3] Di Pietro J.A., Kivlighan K.T., Costigan K.A., Rubin S.E., Shiffler D.E., Henderson J.L. *et al.*: "Prenatal antecedents of newborn neurological maturation". *Child Dev.*, 2010, 81, 115.
- [4] Eldib M., Massaro A.N., Bulas D., Aly H.: "Neuroimaging and neurodevelopmental outcome of premature infants". *Am. J. Perinatol.*, 2010, 27, 803.
- [5] Leijser L.M., Vos N., Walther F.J., van Wezel-Meijler G.: "Brain ultrasound findings in neonates treated with intrauterine transfusion for fetal anaemia". *Early Hum. Dev.*, 2012, 88, 717.
- [6] Pooh R.K.: "Neurosonography by three-dimensional ultrasound". *Semin. Fetal Neonatal Med.*, 2012, 17, 261.
- [7] Whitaker A.H., Feldman J.F., Lorenz J.M., McNicholas F., Fisher P.W., Shen S. *et al.*: "Neonatal head ultrasound abnormalities in preterm infants and adolescent psychiatric disorders". *Arch. Gen. Psychiatry*, 2011, 68, 742.
- [8] Catte L., Keersmaecker B., Claus F.: "Prenatal neurologic anomalies: sonographic diagnosis and treatment". *Paediatr. Drugs.*, 2012, 14, 143.
- [9] Gerdavan W.M., Sylke J.S., Lara M.L.: "Cranial Ultrasonography in Neonates: Role and Limitations". *Semin. Perinatol.*, 2010, 34, 28.
- [10] Nelly F.P., Goya E., Tomas J., Gratacos E., Hernandez-Andrade E.: "Quantitative Tissue Echogenicity of the Neonatal Brain Assessed by Ultrasound Imaging". *Ultrasound Med. Biol.*, 2009, 35, 1421.
- [11] Su Y.J., Du L.F., Wu Y., Zhang J., Zhang X., Jia X., *et al.*: "Evaluation of cervical cancer detection with acoustic radiation force impulse ultrasound imaging". *Exp. Ther. Med.*, 2013, 5, 1715.
- [12] Cui G., Yang Z., Zhang W., Li B., Sun F., Xu C. *et al.*: "Evaluation of acoustic radiation force impulse imaging for the clinicopathological typing of renal fibrosis". *Exp. Ther. Med.*, 2014, 7, 233.
- [13] Hou X.J., Sun A.X., Zhou X.L., Ji Q., Wang H.B., Wei H., *et al.*: "The application of Virtual Touch tissue quantification (VTQ) in diagnosis of thyroid lesions: a preliminary study". *Eur. J. Radiol.*, 2013, 82, 797.
- [14] Mateen M.A., Muheet K.A., Mohan R.J., Rao P.N., Majaz H.M., Rao G.V. *et al.*: "Evaluation of ultrasound based acoustic radiation force impulse (ARFI) and eSie touch sonoelastography for diagnosis of inflammatory pancreatic diseases". *JOP*, 2012, 13, 36.
- [15] Meng W., Zhang G., Wu C., Wu G., Song Y., Lu Z.: "Preliminary results of acoustic radiation force impulse (ARFI) ultrasound imaging of breast lesions". *Ultrasound Med. Biol.*, 2011, 37, 1436.
- [16] Shuang M.T., Ping Z., Ying Q., Li-Rong C., Ping Z., Rui-Zhen L.: "Usefulness of acoustic radiation force impulse imaging in the differential diagnosis of benign and malignant liver lesions". *Acad. Radiol.*, 2011, 18, 810.
- [17] Doherty J.R., Dahl J.J., Trahey G.E.: "Harmonic tracking of acoustic radiation force-induced displacements". *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, 2013, 60, 2347.
- [18] Zhan J., Diao X.H., Chai Q.L., Chen Y.: "Comparative study of acoustic radiation force impulse imaging with real-time elastography in differential diagnosis of thyroid nodules". *Ultrasound Med. Biol.*, 2013, 39, 2217.
- [19] Sporea I., Gilja O.H., Bota S., Şirli R., Popescu A.: "Liver elastography - an update". *Med. Ultrason*, 2013, 15, 304.
- [20] Wojcinski S., Brandhorst K., Sadigh G., Hillemanns P., Degenhardt F.: "Acoustic radiation force impulse imaging with Virtual Touch™ tissue quantification: mean shear wave velocity of malignant and benign breast masses". *Int. J. Womens Health*, 2013, 30, 619.
- [21] Sugitani M., Fujita Y., Yumoto Y., Fukushima K., Takeuchi T., Shimokawa M., *et al.*: "A new method for measurement of placental elasticity: acoustic radiation force impulse imaging". *Placenta*, 2013, 34, 1009.

- [22] Kenichi O., Susumu M., Pamela K.D., Ernst T., Anderson L., Buchthal S., *et al.*: "Multi-contrast human neonatal brain atlas: Application to normal neonate development analysis". *Neuroimage*, 2011, 56, 8.
- [23] Herba C.M., Roza S.J., Govaert P., van Rossum J., Hofman A., Jaddoe V., *et al.*: "Infant Brain Development and Vulnerability to Later Internalizing Difficulties: The Generation R Study". *J. Am. Acad. Child & Adolesc. Psychiatry*, 2010, 49, 1053.
- [24] Steggerda S.J., de Bruïne F.T., Smits-Wintjens V.E., Walther F.J., van Wezel-Meijler G.: "Ultrasound detection of posterior fossa abnormalities in full-term neonates". *Early Hum. Dev.*, 2012, 88, 233.
- [25] Helen B., Chryssoula P., Ioannis N., Basilios T., Euthimia B.A., Goulamos E., *et al.*: "Comparison of findings on cranial ultrasound and magnetic resonance imaging before discharge in preterm infants. Correlation with the neurological examination". *Early Hum. Dev.*, 2010, 86, S29.
- [26] Gross B., Garcia-Tapia D., Riedesel E., Ellinwood N.M., Jens J.K.: "Normal canine brain maturation at magnetic resonance imaging". *Vet. Radiol. Ultrasound*, 2010, 51, 361.
- [27] Tusor N., Arichi T., Counsell S.J., Edwards A.D.: "Brain development in preterm infants assessed using advanced MRI techniques". *Clin. Perinatol.*, 2014, 41, 25.

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