

Table 1 Targeted imaging strategies of NBs.

Targeted imaging strategy	NBs	Reasons for selectivity	Tumor	Ref.
Binding to specific substances	Cyanine 5.5-conjugated NBs (cy5.5-NBs)	Covalent conjugate structure of cy5.5 and NBs	Liver cancer	[46]
	Ultrasonic NBs coupled with specific anti-PSMA (prostate specific membrane antigen) nano-bodies	Antigen-antibody binding	Prostate cancer	[47]
	NBs with biotinylated anti-ErbB2 Affibody® molecules	Binding to receptor HER2	Breast cancer	[48]
	NBs with a phospholipid membrane that can bind to the fluorescent dye NIRF IR-780 iodide	IR-780 iodide is used as a target ligand for tumor uptake	Female tumors	[49]
	NBs of CA-125-targeted echogenic lipid and surfactant-stabilized	Antigen-antibody binding	Ovarian cancer	[50]
Optimize the preparation method of nanobubbles	NBs of uniform size	NBs with uniform size has excellent passive targeting ability in tumors	Colon cancer	[51]
	NBs modified by FOL increase the FOL content in each DSPE-PEG2000 chain	Enhance the binding to folate receptor (FR)	Breast cancer	[52]

**Table 2 The applications of NBs as anti-tumor drug carriers.**

The purpose of drug loading	NBs	Drugs/Gene	Tumor	Ref.
UTND promotes drug release	Lipid NBs	Doxorubicin (DOX)	Prostate cancer	[58]
	GPC3-targeted and apatinib-loaded NBs	Apatinib	Liver cancer	[59]
	G250 antigen-targeting temsirolimus-loaded nanobubbles (G250-TNBs)	Temsirolimus (TEM)	Renal carcinoma	[60]
Improve gene transfection	NBs carrying androgen receptor (AR) siRNA	AR siRNA	Prostate cancer	[62]
	Ultrasonic NBs	Purine nucleoside phosphorylase (PNP)/fludarabine	Liver cancer	[63]
	Poly(lactic-co-glycolic acid) (PLGA) NBs expressing nerve growth factor (NGF) (NGF/PLGA NBs)	Nerve growth factor (NGF)	Spinal cord injuries (SCI)	[65]
	Brain-derived neurotrophic factor (BDNF)-loaded cationic nanobubbles (CNBs) conjugated with MAP-2 antibody (mAb <sub>MAP-2</sub> /BDNF/CNBs)	Brain-derived neurotrophic factor (BDNF)	Spinal cord injuries (SCI)	[66]
Assist radiofrequency ablation of tumors	Gd-C5F12-phospholipid nanobubbles (PLNs)		Colon cancer	[67]
	Lipid-shelled Pluronic NBs		Colorectal adenocarcinoma	[68]



Table 3 The dual-function applications of NBs as imaging contrast agents and anti-tumor drug carriers.

NBs	Reasons for dual function	Drugs	Tumor	Ref.
NBs converted from perfluorocarbon nanodroplets	Drug delivery: NBs; imaging: provided by MB formed by NBs gathered in tumor tissue	Doxorubicin (DOX)	Breast cancer	[99]
NBs composed of 1% of Tween 80, and 3 mg/ml of lipid	Related to the addition of 1% of Tween 80	Coumarin-6	Breast cancer	[100]
NB-based dual contrast enhancement agents encapsulated with perfluoropentane and stabilized with SPIO nanoparticles	SPIO: enhance the contrast of US and MR imaging; magnetic targeting and HIFU: enhance targeting and trigger drug release	Carmustine	Glioma	[101]
NBs wrapped with carbon tetrafluoride gas	Carbon tetrafluoride: ultrasound imaging; ultrasound-mediated NBs: drug delivery and tumor targeting	Doxorubicin (DOX)	Liver cancer	[102]
Nanobubble-paclitaxel liposome (NB-PTXLp) complexes	Drug delivery: US induced cavitation of NBs; imaging: liposomes	Paclitaxel ( PTX )	Breast cancer; head and neck cancer; pancreatic ductal adenocarcinoma	[103]
Glycine/PEG/RGD modified poly(methacrylic acid) NBs	Drug delivery: EPR effect; imaging: PFH	Doxorubicin (DOX)	Renal carcinoma	[104]